Clinical Study Report Synopsis	
Drug Substance	Budesonide/Formoterol
Study Code	D5890L00021
Edition Number	1.0
Date	8 May 2009

TITLE: PHYSICIAN AND PATIENT PERCEPTION OF ADJUSTABLE MAINTENANCE DOSING OF SYMBICORT TURBUHALER (REALITY)

Study dates: First patient enrolled: 5 September 2006
Last patient completed: 3 January 2007

Phase of development: IV

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

The following abbreviations and special terms are used in this study protocol.

Abbreviation or special term	Explanation
ACQ:	Asthma Control Questionnaire
AE:	Adverse Event
DBP:	Diastolic Blood Pressure
GERD:	Gastroesophageal Reflux Disease
NA:	Not Available
SAE:	Serious Adverse Event
SBP:	Systolic Blood Pressure
SD:	Standard Deviation
PRO:	Patient Reported Outocomes

Study centre(s):

41 primary care office-based physicians.

Publications:

Not applicable

Objectives

Primary objective

The main objective of the present study was to evaluate the physicians' and patients' perception about the approved adjustable dosing of Symbicort® 160/4.5 µg.

Secondary objective

To evaluate the easiness of adjustable maintenance-dosing schedule of Symbicort®.

Study design

Prospective, open label, non-randomized, observational, non-interventional study.

Target patient population and sample size

The study sample comprised of 202 asthma patients who qualified to receive Symbicort® according to the local labeling, i.e. patients who require regular treatment for asthma with a combination of an inhaled corticosteroid and a long acting beta-2 agonist.

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

Due to the non-interventional nature of the study no investigational product was supplied in the present study.

All study subjects received maintenance Budesonide/Formotelol (Symbicort®) Turbuhaler 160/4.5 µg. Maintenance dose was titrated (upwards or downwards) within the approved dose range of 1x2 - 4x2 inhalations per day according to the level of asthma symptoms.

No comparator treatments were tested.

Duration of treatment

The duration of patients' observation was 3 months.

Criteria for evaluation - efficacy and pharmacokinetics (main variables)

Primary criteria for evaluation:

- Patients' satisfaction with the adjustable maintenance dosing schedule
- Physicians' satisfaction with the adjustable maintenance dosing schedule

Secondary criteria for evaluation:

- Easiness of adjustable maintenance-dosing schedule of Symbicort®

Patient-reported outcomes (PROs)

Study subjects completed the ACQ (Asthma Control Questionnaire) during the study (Visits 1-3).

Criteria for evaluation - safety

Any AE/SAE recorded during the study period.

Statistical methods

Statistical analysis was based on summary statistics by visit.

Data analysis set was based on the Intention-to-Treat-Population (all patients entered in the study who received at least one dose of study medication).

Summary of results

Two hundred and two (202) patients were enrolled in the current study. One hundred and eighty seven (187) patients (92.6%) completed the study. Thirteen patients (13) had only baseline (Visit 1) data available, while another 2 patients had only Visit 1 & Visit 2 data available.

Baseline characteristics of the study population are summarised in table 1.

Table 1. Baseline Characteristics of the study population

Sex	Male	41.1%
	Age*	50.1±17.9 yrs
	Weight*	76.4±15.7 kgr
	SBP*	125±16.3 mmHg
	DBP*	80.6±10.2 mmHg
	Pulse*	78.0±8.5 beats/min
Asthma Severity	Mild persistent	40.1%
	Moderate persistent	54.2%
	Severe persistent	5.7%
Co-morbidities	Yes	36.5%
	Arterial Hypertension	14%
	Allergic Rhinitis	5%
	Dyslipidaemia	4%
	Coronary Heart Disease	2%
	Diabetes Mellitus	2%
	GERD	1%

**Values are expressed as mean±sd.*

Primary Endpoints

Patient Satisfaction

Study subjects completed the ACQ questionnaire throughout the study (Visits 1, 2, 3). The first 5 questions were used to calculate the total ACQ-5 score.

Mean total ACQ-5 score was gradually improved from Visit 1 to Visit 3 (table 2).

Table 2. ACQ-5 score by visit

	Visit 1		**Visit 2**		**Visit 3**	
	N	**Mean±SD**	**N**	**Mean±SD**	**N**	**Mean±SD**
ACQ-5 score	155	2.2±1.1	155	1.2±0.8	156	0.7±0.6

The analysis of each individual ACQ question is illustrated in figures 1-5.

Figure 1. Night Awakening

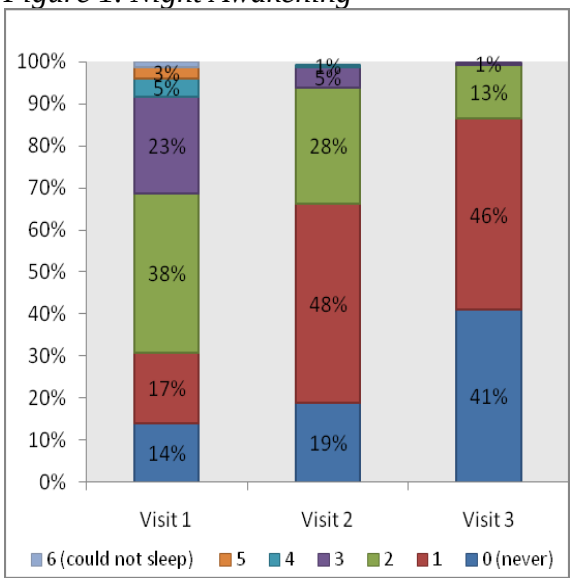


Figure 2. Morning Symptoms

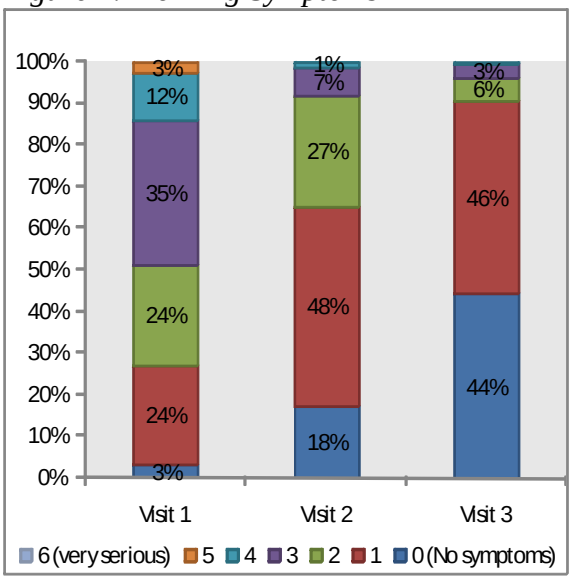


Figure 3. Activity Limitation

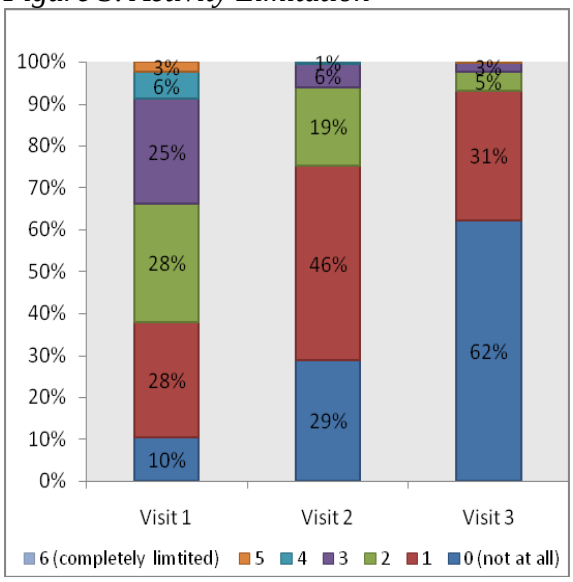


Figure 4. Shortness of breath

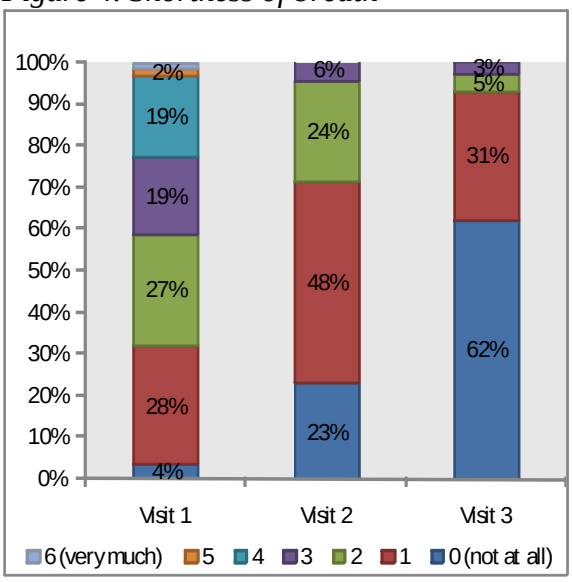
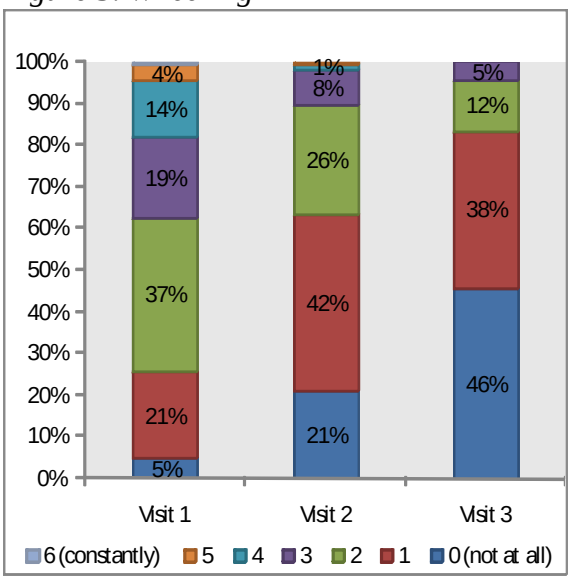


Figure 5. Wheezing



Physician Satisfaction

Participating investigators completed a 4-point evaluation question on their personal assessment regarding response to treatment. According to investigators' assessment at Visit 3, 90.2% of patients showed improvement and significant improvement in terms of their condition, whereas asthma deterioration was reported only in 2.2% (table 3).

Table 3. Response to treatment according to the investigators

	Visit 2		Visit 3	
	N	**%**	**N**	**%**
Significant improvement	77	41.4	106	57.6
Improvement	98	52.7	60	32.6
No change	8	4.3	14	7.6
Deterioration	3	1.6	4	2.2
Total	186		184	
NA	*16*		*18*	

Secondary Endpoints

Easiness of the adjustable maintenance dosing schedule of Symbicort®

Based on a 5-point evaluation scale, the vast majority of patients were convenient with the adjustable maintenance-dosing schedule. Namely, 94.5% and 97.3% of patients found it "easy" and "very easy" at Visits 2 and 3 respectively (table 4).

Table 4. Easiness of adjustable maintenance dosing schedule of Symbicort®

	Visit 2		Visit 3	
	N	**%**	**N**	**%**
Very easy	110	60.4	127	69.8
Easy	62	34.1	50	27.5
Not easy but not difficult	10	5.5	5	2.7
Difficult	0	0	0	0
Very Difficult	0	0	0	0
Total	182		182	
NA	*20*		*20*	

Other variables – Use of reliever medication

Requirement for reliever medication was reduced during the study (ACQ question 6), as illustrated in table 5.

Table 5. Inhalations of reliever medication

	Visit 1		Visit 2		Visit 3	
	N	**%**	**N**	**%**	**N**	**%**
No inhalations	50	32.5	92	59.4	121	78.6
1-2 most of the days	58	37.7	49	31.6	32	20.8
3-4 most of the days	33	21.4	12	7.7	1	0.6
5-8 most of the days	10	6.5	2	1.3	0	0
9-12 most of the days	3	1.9	0	0	0	0
Total	154		155		154	
NA	*48*		*47*		*48*	

Other variables –Dose adjustments

At Visit 2 dose was increased in 8 out of 189 patients and decreased in 49 of 189.

At Visit 3 dose was increased in 5 out of 185 patients and decreased in 65 out of 187.

Other variables –Treatment failures

According to the study protocol treatment failure defined as:

- asthma related SAE
- hospitalisation due to asthma deterioration
- use of emergency medication
- *per os* administration of corticosteroids for at least 5 days due to asthma deterioration.
- any patient withdrawal resulting in treatment alteration due to poor response.

Twelve (12) patients presented with “treatment failure” as defined in the study protocol:

- One (1) patient was hospitalized due to asthma deterioration and also received emergency medication for 15 days as well as oral corticosteroids for 5 or more days.
- Five (5) patients received emergency medication and oral corticosteroids for 5 or more days.
- Two (2) patients received emergency medication.
- Four (4) patients presented 2 “treatment failure” episodes.

In total 16 “treatment failure events” were reported in 12 patients:

- 15 events of emergency medication use for 6.6±3.3 days (mean±sd).
- 12 events of *per os* administration for 5 days or more due to asthma deterioration.

Safety Analysis

One patient experienced tachycardia during the study. The event was reported as mild and eventually recovered. One patient (no. 302) was reported to have been hospitalised due to asthma deterioration.

Summary of pharmacokinetic results

Not applicable

Summary of pharmacodynamic results

Not applicable

Summary of pharmacokinetic/pharmacodynamic relationships

Not applicable

Summary of pharmacogenetic results

Not applicable