AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Various commercially available ICS/LABA with or without as needed SABA
ACTIVE INGREDIENT: short-acting β_2-agonist (SABA), long-acting β_2-agonist(LABA), inhaler glucocorticosteroid (ICS).
(ex. Fixed combination inhalers therapy : fluticasone propionate plus salmeterol, budesonide plus formoterol)

Study No: NIS-RTW-SYM-2008/1
Real life effectiveness in patients with not optimally controlled asthma: Symbicort SMART, or other ICS/LABA with as needed SABA

Developmental Phase: IV
Study Completion Date: 12 May 2011
Date of Report: 30 Nov 2011

OBJECTIVES:

We aimed at conducting a non-interventional study to explore actual asthma control status in real-life environment and to observe the efficacy after stepped-up to Symbicort SMART or various identical regimens.

Primary objectives

To observe the efficacy after stepped-up to Symbicort SMART or various identical regimens by the change of ACQ score from baseline.

Secondary objectives

- To observe the change of asthma control status from enrolment
- To observe the change of pulmonary function
- To observe the medical resource utilization

METHODS:

This was an observational, multi-center study started with identifying asthma control status among patients who seek for treatment at investigators' clinics. Screening process

based on GINA guideline were conducted and supported by patient's self-assessment of Asthma Control Questionnaire (ACQ).

The step up therapeutic regimens prescribed (e.g., Symbicort SMART or others) were documented and the efficacy were followed up upon returned visits. Patients who need to prescribe oral corticosteroids based on discretion of physicians within study period were unnecessarily to be withdrawn.

The data/questionnaire collected at enrollment and follow-up period included ACQ, usage/dose of reliever/ICS, pulmonary functions, and number of unscheduled clinic visits, emergency room visits and hospitalization for exacerbations. Asthma maintenance period prior to enrollment was also recorded in the CRF. Timeframe for follow up visits was at week 4 and week 12~16 (if applicable) according to the regular institutional schedule. Telephone contacts to prolong the follow-up in medical resource utilization (ER/clinic visits for exacerbations) were at 6 and 12 months.

Throughout study period, patient diary cards were collected and patient education to optimize adoption on various devices/inhalers was provided based on materials routinely used in clinics.

RESULTS:

Among the full analysis set, 551 patients received Symbicort and 172 patients received Seretide at baseline. There were 358 patients receiving Symbicort and 130 patients receiving Seretide had a visit at Week 12~16. A total of 488 patients complete the study.

Demographic

Among the full analysis set, 48.13% were male and 51.87% were female. The average age was 55.77±16.54 years old, ranging from 11.0 to 93.0 years old. The mean height was 160.78±8.37 cm and the mean weight was 64.54±11.96 kg. 72.5% was partly controlled asthma patients and 27.5% was uncontrolled asthma patients. The proportions of the following medical events within the past 3 months were reported by patients: 32.64% had exacerbation; 16.60% had unscheduled clinic visit; 8.02% had attended ER; 2.63% had been hospitalized and the average hospitalization duration was 0.24±1.76 days.

Change of ACQ

The Asthma Control Questionnaire (ACQ) measures both the adequacy of asthma control and change in asthma control, which occurs either spontaneously or as a result of treatment. The full analysis set had mean ACQ score of 1.52±1.11 at baseline. The mean ACQ score significantly decreased to 0.78±0.88 at Week 4 and further decreased to 0.61±0.81 at Week 12~16. The change of ACQ score from baseline was -074±1.10 at Week 4 and was -0.85±1.18 at Week 12~16. The mean ACQ score significantly decreased (more than 0.5) after 4 weeks of asthma treatment; however, no significant difference was observed between the two subgroups.

Change of Asthma Controlled Status

The controlled rate in patients receiving Symbicort (56.1%) was significant higher than patients receiving Seretide (43.6%) in overall population at the end of study (p-value=0.0050). However, improvement rate at the end of study did not demonstrate a significant difference between the two subgroups (66.5% vs. 60.8%). Furthermore, the

controlled rate at the end of study was 59.1% in partly controlled patients receiving Symbicort and was 50.9% in partly controlled patients receiving Seretide. The controlled rate favored patients receiving Symbicort but was not significant. Consequently, the controlled rate at the end of study was 47.6% in uncontrolled patients receiving Symbicort and was 28.6% in uncontrolled patients receiving Seretide. The controlled rates were significant different (p-value=0.0168). The result indicated that patients with partly controlled or uncontrolled asthma had a higher chance to control their asthma by using Symbicort.

Change of Pulmonary Function

Lung function tests evaluated the improvement of lung function. The mean FEV1 showed a 0.02±0.18 liter significant increase in patients receiving Symbicort (p-value=0.0492) at the end of study; however, the mean FEV1 did not showed a significant change from baseline in patients receiving Seretide. Moreover, the increase was primarily contributed by partly controlled patients in Symbicort group with a mean increase in FEV1 of 0.03±0.17 liter (p-value=0.0056). Other treatment subgroups did not show a significant change. Similarly, FEV1/FVC ratio showed a significant increase of 0.94±4.96% from 78.07±18.58% at the end of study in the full analysis set (p-value=0.0016) and showed a significant increase in patients receiving Symbicort (p-value=0.0079) and in partly controlled patients receiving Symbicort (p-value=0.0127). Likewise, PEF ratio showed a significant increase of 10.83±55.37 liter/min from 304.60±123.44 liter/min at the end of study in the full analysis set (p-value=0.0005) and showed a significant increase in patients receiving Symbicort (p-value=0.0003), in partly controlled patients receiving Symbicort (p-value=0.0083) and in uncontrolled patients receiving Symbicort (p-value=0.0128). In summary, patients receiving Symbicort showed measurable improvement in lung function.

Medical Resource Utilization

Medical resource utilization due to asthma was recorded and analysis. The incidences were very low. In detail, the incidence of exacerbations was 0.221 person-year; the incidence of unscheduled clinic visit was 0.179 person-year; the incidence of emergency room visit was 0.012 person-year; the incidence of hospitalization was 0.074 person-year; and the incidence of usage of oral CS treatment was 0.047 person-year. Low utilization of medical resource was also observed with asthma treatment during the study.

Compliance

The compliance of the asthma treatment in both subgroups were high, approximately 90%, and only a few proportion of patients changed their asthma treatment during the study.