Conclusion Report of Non-interventional Study(NIS)

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The asthma control rate achieved by budesonide/formoterol in clinical practice in China

Study duration:	**Date of first subject in: 09 May 2013** **Date of last subject last visit: 14 October 2014**

Conclusion Report Synopsis of Non-interventional Study

Study Title: The asthma control rate achieved by budesonide/formoterol in clinical practice in China

Study period:

Date of first subject in: 9 May 2013

Date of last subject last visit: 14 Oct 2014

Study objectives:

Primary objective: To get the asthma control rate data achieved by budesonide/formoterol combination therapy in clinical practice in Chinese asthma patients by evaluation of controlled and partly controlled asthma rate according to GINA definition.

Secondary objective: To get the asthma control rate data achieved by budesonide/formoterol combination therapy in clinical practice in Chinese asthma patients by evaluation of completely controlled and well controlled asthma rate according to ACT score.

Study design:

This was a multi-centre, cross-sectional study conducted in China. There was only one visit in this study. Informed consent and all following study procedures (ACT, clinical assessments) aligned with hospital's clinical practice were done and completed at this visit.

Study sites and number of patients:

In this study, patients were enrolled at a total of 27 sites. It was planned that 1500 patients would be enrolled. Actually, 1502 patients were enrolled.

Selection of subject population:

Inclusion criteria:

（1） Signed the informed consent form;

（2） Outpatient, female or male aged 18 years and over;

（3） Clinical diagnosis of asthma at least 6 months;

（4） Prescribed with budesonide/formoterol treatment at least 3 months before enrollment;

（5） Had used the same maintenance dose of budesonide/formoterol for at least 4 weeks before enrollment;

（6） Could correctly use Turbuhaler® and had good compliance with prescription judged by investigator;

Exclusion criteria:

（1） Participation in any clinical study within 3 months;

（2） Had COPD history/suspicious COPD;

（3） ≥ 10 pack years of smoking history;

（4） Used any other asthma maintenance medication accompanied with budesonide/formoterol within 3 months before enrollment;

（5） With asthma acute attack (defined as asthma symptom deterioration resulting in oral/rectal/parenteral GCS medication or emergency room treatment or hospitalisation) within 4 weeks before enrollment;

Statistical analysis:

Estimation of sample size:

According to previous studies, the control rate achieved by budesonide/formoterol was 75.9% (control + partial control based on GINA definition, SMARTASIA Study, Asia population, data on file), 68.3% (control + partial control based on GINA definition, SMARTASIA Study, Chinese population, data on file) and 86.5% (ACT≥20, NIS-RTH-SYM-2008-1 Study in Thailand, data on file), respectively. If control rate achieved by ICS/LABA therapy was 68.3% (since the study population was Chinese asthma patients), then the length of 95% CI was ±2.4% with 1500 patients based on normal approximation.

Population for analysis:

Full Analysis Set (FAS) was the primary analysis set. All enrolled asthma patients received budesonide/formoterol treatment except screening failures were included in the FAS.

General statistical principles:

SAS statistical analysis software, Version 9.2, was used for statistical analysis.

The continuous variables were described using number, mean, standard deviation, median, minimum and maximum. The decimal digits of minimum and maximum were consistent with source data documented in the database. One more decimal place was kept for mean and median compared to source data recorded in database, and two more decimal places for standard deviation, however, at most four decimal places were kept.

The qualitative variables were described using frequency, percentage and number of missing data, respectively. If the count was zero, only "0" was presented. Percentage was calculated based on non-missing data. The percentage was calculated to one decimal place.

95% confidence intervals were constructed for the efficacy analyses. All 95% confidence intervals were based on normal theory method.

Efficacy analysis:

Primary variables:

The primary variable of this study was the rate of controlled and partly controlled asthma according to GINA definition.

Calculate the constituent ratios of controlled, partly controlled and uncontrolled asthma according to GINA definition.

Calculate the rate of controlled asthma according to GINA definition and 95% confidence interval.

Calculate the rate of partly controlled asthma according to GINA definition and 95% confidence interval. The rate of partly controlled asthma was defined as the proportion of the number of patients with controlled and partly controlled asthma to the total number of patients.

Secondary variables:

（1） The rate of completely controlled and well controlled asthma according to ACT score;

Calculate the constituent ratios of completely controlled, well controlled and uncontrolled asthma according to ACT score;

Calculate the rate of completely controlled asthma according to ACT score and 95% confidence interval;

Calculate the rate of well controlled asthma according to ACT score and 95% confidence interval. The rate of well controlled asthma was defined as the proportion of the number of patients with completely controlled and well controlled asthma to the total number of patients.

（2） The average frequency of reliever use within one week before enrollment

The average frequency of reliever use within one week before enrollment was described using number, mean, standard deviation, median, minimum and maximum. Meanwhile, this

variable was summarized based on five categories (0, 1, 2, 3 and not less than 4 times). Patients adopting fixed dose strategy and SMART strategy were separately described.

Results and conclusion:

Results:

Demographic characteristics:

This study enrolled 1502 asthma outpatients at 27 study sites, among which, 1483 patients enrolled were eligible.

Demographic characteristics showed that the average age of patients was 43.6 years (ranged from 18 to 84 years). There were more female than male patients, including 954 female patients (64.3%) and 529 male patients (35.7%). The majority of patients enrolled had education of secondary school, university and above. Among patients enrolled, 24 patients (1.6%) were illiterate, 210 patients (14.2%) had education of primary school, 706 patients (47.6%) had education level of secondary school, and 543 patients (36.6%) had education of university and above. As for dwelling environment, 362 patients (24.4%) were from rural areas and 1121 patients (75.6%) were from city.

Smoking status:

1308 (88.2%) patients never smoked and 175 patients (11.8%) had smoking history, including 38 patients (2.6%) who were smoking at enrolment and 137 patients (9.2%) who had smoked before enrolment. The average smoking index of patients who had smoking history was 4.66 (range: 0.1~9.8).

Asthma medical historyand histories of other important diseases:

The average disease course of asthma for patients was 6.15 years (range: 0.5~59.7 years). The disease course was less than 2 years for 729 patients (49.2%), 2~5 years for 276 patients (18.6%) and over 5 years for 478 patients (32.2%).

In addition to asthma, a total of 585 patients (39.4%) had other important diseases. The most commonly reported comorbidities included allergic rhinitis (20.7%, 307/1483), hypertension (7.6%, 112/1483), diabetes mellitus (2.5%, 37/1483) and coronary artery disease (1.2%, 18/1483).

Therapeutic medication:

The average treatment duration of budesonide/formoterol was 15.67 months (range: 2.7~150.5 months).

Among three dosages of budesonide/formoterol for inhalation, the most commonly used dosage was 160μg/4.5μg (97.0%, 1439/1483), the others were 80μg/4.5μg (2.7%, 40/1483) and 320μg/9μg (0.3%, 4/1483). The most common administration was 1 inhalation/time, twice daily, accounted for 71.4% (1028/1439), 77.5% (31/40) and 100.0% (4/4) for dosages of 160μg/4.5μg, 80μg/4.5μg and 320μg/9μg, respectively.

The average treatment duration of current budesonide/formoterol dosage was 10.27 months (range: 0.9~150.5 months). Treatment duration with the current dose was less than 3 months for 183 patients (12.3%) , 3~6 months for 609 patients (41.1%) , 6~12 months for 374 patients (25.2%), 1~3 years for 242 patients (16.3%) and over 3 years for 75 patients (5.1%).

At enrollment, 217 patients (14.6%) were using budesonide/formoterol with fixed dose strategy, 1266 patients (85.4%) with SMART strategy.

Lung function test results before budesonide/ formoterol treatment:

In this study, bronchial dilatation test results before budesonide/formoterol treatment of 49 patients (3.3%) were obtained, the average FEV_1 before the use of bronchodilator was 1.749L (range: 0.55~4.16L), the average FEV_1 after the use of bronchodilator was 2.030L (range: 0.75~4.64L), and the average ventilation improvement rate was 16.1%. The average FEV_1% predicted normal before the use of bronchodilator was 58.655% (range: 18.40%~101.10%), the average FEV_1% predicted normal after the use of bronchodilator was 67.377% (range: 2.66%~106.40%), and the average ventilation improvement rate was 14.9%.

Among 95 patients (6.4%) who had lung function test results, the average FEV_1 was 2.193L (range: 0.68~4.61L), the average FEV1% predicted normal was 77.921% (range: 27.90%~132.30%).

Rate of controlled and partly controlled asthma according to GINA definition:

In this study, the rate of controlled asthma was 58.6% (95%CI: 56.05%~61.13%), and the rate of controlled and partly controlled asthma was 94.1% (95%CI: 92.80%~95.27%).

Among 1483 patients, except 2 patients with missing records, the asthma status was clinically evaluated as controlled for 868 patients (58.6%), partly controlled for 526 patients (35.5%), and uncontrolled for 87 patients (5.9%).

Subgroup analyses:

The rates of controlled asthma of male and female patients were 54.0% (95%CI: 49.62%~58.29%) and 61.2% (95%CI: 58.00%~64.28%), respectively. The rate of controlled asthma of female patients was significantly higher than that of male patients (P=0.0071). The rates of controlled and partly controlled asthma of male and female patients were 92.0% (95%CI: 89.40%~94.21%) and 95.3% (95%CI: 93.73%~96.54%), respectively. The rate of controlled and partly controlled of female patients was also significantly higher than that of male patients (P=0.0113).

In three groups of patients aged less than 30 years, 30~50 years and over 50 years, the rates of controlled asthma were 68.8% (95%CI: 62.66%~74.49%), 60.3% (95%CI: 56.72%~63.71%) and 50.1% (95%CI: 45.40%~54.82%), respectively. There was statistically significant difference (P=0.0000) in comparison between groups, indicating that the rate of controlled asthma in the group with young age was significantly higher than that of group with old age. The rates of controlled and partly controlled asthma were 96.8% (95%CI: 93.79%~98.61%), 93.5% (95%CI: 91.49%~95.09%) and 93.8% (95%CI: 91.15%~95.84%), respectively. There was no statistically significant difference (P=0.1390) in comparison between groups.

In three groups of patients who had disease course less than 2 years, 2~5 years and over 5 years, the rates of controlled asthma were 69.1% (95%CI: 65.60%~72.44%), 55.8% (95%CI: 49.72%~61.75%) and 44.2% (95%CI: 39.72%~48.82%), respectively. There was statistically significant difference (P=0.0000) in comparison between groups. The rates of controlled and partly controlled asthma were 97.4% (95%CI: 95.95%~98.42%), 93.5% (95%CI: 89.89%~96.09%) and 89.5% (95%CI: 86.41%~92.12%), respectively. There was also statistically significant difference (P=0.0000) in comparison between groups. The results showed that the rate of controlled and partly controlled asthma in patients with short disease course was significantly higher than that of patients with long disease course.

The rates of controlled asthma were 52.6% (95%CI: 45.96%~59.11%), 53.3% (95%CI: 49.50%~57.00%) and 68.1% (95%CI: 64.04%~72.04%) in three groups of patients who had education of primary school and below, secondary school and university and above, respectively. There was statistically significant difference (P=0.0000) in comparison between

groups. The rate of controlled asthma in the group with high level of education was significantly higher than that of group with low level of education. The rates of controlled and partly controlled asthma were 91.9% (95%CI: 87.61%~95.04%), 93.5% (95%CI: 91.38%~95.18%) and 95.9% (95%CI: 93.93%~97.44%), respectively. There was no statistically significant difference (P=0.0510) in comparison between groups.

The rate of completely controlled and well controlled asthma according to ACT score:

In this study, the rate of completely controlled asthma was 22.4% (95%CI: 20.29%~24.60%). The rate of well and completely controlled asthma (ACT≥20) was 83.3% (95%CI: 81.35%~85.21%).

The average ACT score of patients was 22.0 (range: 6~25). Among 1483 patients, the asthma status of 332 patients (22.4%), 904 patients (61.0%) and 247 patients (16.7%) were evaluated as completely controlled, well controlled and uncontrolled, respectively.

Subgroup analyses:

The rate of completely controlled asthma of male and female patients were 19.1% (95%CI: 15.83%~22.71%) and 24.2% (95%CI: 21.53%~27.06%), respectively. The rate of completely controlled asthma of female patients was significantly higher than that of male patients (P=0.0234). The rate of well and completely controlled asthma of male and female patients were 80.0% (95%CI: 76.29%~83.29%) and 85.2% (95%CI: 82.81%~87.41%), respectively. The asthma control of female patients was also significantly better than that of male patients (P=0.0092).

In three groups of patients aged less than 30 years, 30~50 years and over 50 years, the rates of completely controlled asthma were 24.7% (95%CI: 19.49%~30.52%), 21.4% (95%CI: 18.56%~24.43%) and 22.8% (95%CI: 19.04%~26.99%), respectively. There was no statistically significant difference (P=0.5274) in comparison between groups. The rates of well and completely controlled asthma were 85.7% (95%CI: 80.70%~89.75%), 82.8% (95%CI: 80.01%~85.42%) and 82.9% (95%CI: 79.13%~86.28%), respectively. There was no statistically significant difference (P=0.5583) in comparison between groups.

In three groups of patients who had disease course less than 2 years, 2~5 years and over 5 years, the rates of completely controlled asthma were 29.4% (95%CI: 26.07%~32.81%), 16.7% (95%CI: 12.47%~21.60%) and 15.1% (95%CI: 11.98%~18.59%), respectively. There

was statistically significant difference (P=0.0000) in comparison between groups. The rates of well and completely controlled asthma were 89.4% (95%CI: 86.98%~91.57%), 77.9% (95%CI: 72.54%~82.65%) and 77.2% (95%CI: 73.17%~80.88%), respectively. There was also statistically significant difference (P=0.0000) in comparison between groups. The results showed that asthma control of patients with short asthma disease course were significantly better than that of patients with long disease course.

In three groups of patients who had education of primary school and below, secondary school and university and above, the rates of completely controlled asthma were 19.2% (95%CI: 14.39%~24.87%), 21.0% (95%CI: 18.02%~24.15%) and 25.6% (95%CI: 21.98%~29.49%), respectively. There was no statistically significant difference (P=0.0676) in comparison between groups. The rates of well and completely controlled asthma were 82.5% (95%CI: 76.99%~87.12%), 81.3% (95%CI: 78.23%~84.11%) and 86.4% (95%CI: 83.20%~89.15%), respectively. There was no statistically significant difference (P=0.0542) in comparison between groups.

The average frequency of reliever use within one week before enrollment:

The average frequency of reliever use of patients within one week before enrollment was 0.3 times (range: 0~14 times), among which, 1291 patients (87.1%) did not use reliever, 65 patients (4.4%) used once, 58 patients (3.9%) used twice, 29 patients (2.0%) used three times, 40 patients (2.7%) used four or more times.

Reporting date: 5 May 2015