STUDY REPORT SUMMARY (ABSTRACT)

Sponsor: AstraZeneca China

Title of Study:

The severity of newly diagnosed asthma patients and the result of initial 12weeks treatment in China

Study period: Initiation date: June 2014 Completion date: September 2016

Study objective:

Primary objective:

To evaluate the severity of newly diagnosed asthma patients based on GINA severity category (GINA 2006 update).

Secondary objectives:

To understand asthma medication distribution by category and evaluate the control level of initial 12 weeks treatment.

Study methods: Multi-centre, prospective non-interventional study

Number of patients: Estimated enrollment number was 5000. Actual total of the enrolled patients was 4817.

Inclusion and exclusion criteria:

Inclusion criteria

The subject population that were observed in the NIS, must fulfil all of the following criteria:

1. Newly diagnosed asthma patients who were not on inhaled gluococorticosteroid within 3 months.

2. Out-patients with an age of 18 years and above

3. Signed and dated informed consent

The prescription of the medicinal product was clearly separated from the decision to include the subject in the NIS. Generally, asthma medication refers to those recommended in GINA guideline (GINA2012 update) and decided by investigator.

Patients meeting the eligibility criteria should be successively recruited by investigators. Once a patient agreed to participate in the study, the investigator would

ask the patients to sign an Informed Consent Form.

Exclusion criteria

Patients were not eligible to participate if any of following exclusion criteria was present:

1. Participating in any clinical trial during the last 90 days
2. Have COPD
3. With asthma exacerbation

Statistical analysis:

Statistical analysis data set

Full Analysis Set (FAS) was the primary analysis set. All enrolled asthma patients, except the screening failure patients, i.e., those who meet the inclusion criteria and exclusion criteria and withdraw from the study once the informed consent was given, was included in the FAS.

Population completed study within (12±1) weeks was defined as patients completed study within the 12±1 weeks visit window in Full Analysis Set.

Statistical analysis method

General Aspects

Statistical analyses were performed using Version 9.2 (or newer) of SAS .

Two-sided statistical test was used at the 0.05 significance level,

Continuous variables including age, weight, height, BMI, smoking index and respiration were summarized using n (sample size), missing (missing number), mean, SD, median, Q1, Q3, min, max and Q3-Q1 by baseline severity level.

Distribution of asthma severity level (overall, and five dimensions) was described as categorical variables.

Distribution of Asthma Control Status (), exacerbations (), asthma medication at visit 1 and ACQ-5 (≤0.75, 0.75-1.5, >1.5) () was summarized.

Distribution of asthma medication at each visit by drug class and asthma control status was described by presenting the frequency and percentage of patients in each category.

Continuous variables were analysed with ANOVA or No parameter test and Categorical variables were analysed with Fisher test or Chi-square test. Univariate logistic regression was also used as univariate analysis. The variable which P-value was less than 0.15 in univariate analysis was included in multivariable logistic regression analysis.

Result:

Primary objective of this study was to evaluate the severity of newly diagnosed asthma patients based on GINA severity category (GINA 2006 update).

4817 patients were enrolled into this study, and 4492 of them who met the inclusion and exclusion criterion were included in the FAS. In FAS population, 173（3.85%）patients were intermittent, 538 (11.98%) patients were mild persistent, 1031 (22.56%) patients were moderate persistent, 2767 (61.61%) patients were severe persistent.

Secondary objectives of this study were to understand asthma medication distribution by category and evaluate the control level of initial 12 weeks treatment

1. *Asthma Control Status after 12 weeks treatment*

In FAS population, 3587 (79.87%)patients who completed study had evaluated 12 weeks asthma control status. 1778 patients achieved asthma controlled, accounting for 67.8%, 768 patients were partly controlled, accounting for 29.3%, 77 patients remain uncontrolled, accounting for 2.9%. The control status improved significantly since medication therapy, and the proportion of asthma controlled, partly controlled and uncontrolled at baseline were 6.1%, 50.4%, 43.5% respectively. Through 12 weeks of treatment, the controlled status showed an improvement trend. The patients achieved controlled were 42.89% (462/1075) at week 4, 53.78% (420/781) at week 8 and 67.78% (1778/2623) at week 12. On the contrary, the patients with partly controlled and uncontrolled were decreasing over time.

Meanwhile this study evaluated asthma control status refers to GINA 2016 which update the criterion exclude lung function. And 2833 patients achieved asthma

controlled, accounting for 78.98%, 668 patients were partly controlled, accounting for 18.62%, 86 patients remain uncontrolled, accounting for 2.4%. The control rate was better than evaluated by GINA 2012. There was the same improved trend of asthma control status as GINA2012.

2. *ACQ-5 Questionnaire*

In FAS population, Patients at baseline, week 4, week 8 and week 12 had mean ACQ-5 scores of 1.74, 0.70, 0.46 and 0.36, respectively. During the whole course of the study, the number of patients with a score below 0.75 showed an increasing trend. The percentage was 15.15% (680/4492) at baseline, 61.14% (2545/4017) at week 4, 74.92% (2793/3728) at week 8 and 80.60% (2891/3587) at week 12. On the contrary, the number of patients with a score between 0.75 and 1.5 and patients with a score above 1.5 were decreasing over time. Significant clinical improvement (ACQ score change ≥0.5) from baseline was seen in 71.8% (2881), 80.8% (3014), and 82.9% (2973) of patients at Week 4, Week 8, and Week 12, respectively (paired t-test, $p < 0.0001$). The significant improved from baseline to week 4. It indicated ACQ-5 would improve if got regular medication treatment once.

3. *Drugs distribution*

In FAS population, the top 5 medication prescribed at initial treatment was ICS/LABA90.2%(4051/4491), LTRA 62.1%(2788/4491), THO 14.32%(643/4491) SABA11.4%(512/4491) and LAMA/SAMA 7.88%(354/4491)

Among them, the proportion of ICS/LABA initial as single treatment was 23.47%(1054/4491), LTRA without ICS/LABA was 7.39%(332/4491)

Drug Combination: In FAS as the most common combination drug prescribed with ICS/LABA treatment with LTRA 54.69% (2456/4491), followed by THO 13.2%(593/4491). The combination treatment used most in severer asthma, ICS/LABA+LTRA 67.38%(1655/2456); ICS/LABA+THO 70.49%(418/593)

4. *Exacerbations*

In FAS, there were 96 (2.14%) patients who had at least one exacerbation during the study. Among them, 78 patients had emergency visit, 14 (0.31%) patients used systemic glucocorticosteroids for equal or more than 3 days, and 14 patients were hospitalized. Of the severe persistent patients initially prescribed ICS/LABA, 2.5% experienced an exacerbation compared with 3.1% of those who were not, which verified ICS/LABA could reduce exacerbation in clinical practice.

5. *Risk Factors for Control Status*

The major risk factors significantly associated with control status ($P < 0.05$) were baseline asthma severity categories, compliance (good or poor), gender, occupation. Means that patients once diagnosed asthma need to visit physicians as early as possible and increasing their compliance to treatment are key factors to improve control levels.

6. *Lung function in this study*

The mean of FEV1% normal predicted value was 82.66%, 86.90%, 87.77% and 91.88% at week 0, week 4, week 8 and week 12. The proportion of FEV1%>80% was 60.76%, 68.71%, 73.62%, 79.09% at week 0, week 4, week 8 and week 12. Bronchial Dilation Test was taken at the baseline, and the mean of FEV1 was 328.58ml (±196.98), mean of FEV1% was 19.96%(±14.56%).

Conclusion:

- This study achieved evaluating the severity of 4492 newly diagnosed asthma patients based on GINA severity category (GINA 2006 update) in China. Intermittent accounted for 3.85%, mild accounted for 11.98%, moderate accounted for 22.56% and severe asthma accounted for 61.61%.
- Asthma controlled status improved significantly after 12 weeks treatment. Controlled asthma increased from 6.1% at baseline to 67.8% at Week 12.
- Significant clinical improvement of ACQ-5 when got regular medication treatment once.

- The most popularly initiated medicine is ICS/LABA (90.23%). ICS/LABA could reduce severe asthma exacerbation in clinical practice.
- The major risk factors for control status were asthma severity categories, compliance, gender and occupation.

Report date: September 06, 2017