AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: None
ACTIVE INGREDIENT:

Study No: NIS-RBG-ATC-2012/1; NCT01703416
CORRELATION BETWEEN PATIENT PERCEPTION OF THE ABILITY TO PERFORM MORNING ACTIVITIES AND FINDINGS ON CLINICAL EXAMINATION IN COPD PATIENTS – RELIEF STUDY

Developmental Phase: Non-Interventional Study
Study Completion Date: 01/04/2013
Date of Report: 20/03/2014

Study type

This was a multi-center, prospective, non-interventional study to evaluate, in daily clinical practice, systematic treatment for 12 weeks of combined therapy (LABA/ICS) administered in COPD patients groups C and D, according to GOLD Guidelines Revised 2011. The study consisted of a Baseline visit and 3 follow-up visits.

OBJECTIVES:

(a) Primary objective

To evaluate if there is positive correlation between improvement on the CDLM score and improvement of the general health status visual scale (assessed by clinician during the regular physical exam).

(b) Main secondary objectives

1. To evaluate the percentage of patient which register improvement, using CDLM and general health status visual scale.

2. To evaluate adherence to ICS/LABA treatment in general in COPD patients based on group C and D categorization according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) Guidelines Revised 2011. Group C patients are those with high risk and few symptoms; Group D patients have high risk and more symptoms.

3. To evaluate the effort tolerance of patients with COPD, group C and D according to GOLD Guidelines Revised 2011, by using a pedometer to measure the dynamics of daily walking distance.

4. To evaluate the incidence and impact of COPD exacerbation during the study.

METHODS:

Approximately 50 specialists enroll approximately 500 patients. Each investigator enrolled an average of 10 patients.

All information related to eligible patients was recorded by the health care professionals in Case Report Forms (CRF). Patients brought the completed CDLM questionnaires to the Study Investigators during office visits.

Target subject population

Target subject population is represented by patients:

- Diagnosed with COPD, group C and D, according to GOLD Guidelines Revised 2011 (see Appendix E)
- Aged at least 40 years
- Receiving inhaled combined therapy (inhaled corticosteroid/long acting $ß_2$-agonist bronchodilator), no matter which treatment, according to indications approved in SPC
- Accepting to use a pedometer and to record the number of steps

Diagnosis and Main Criteria for Inclusion: Patients in the study were aged 40 years of age or older diagnosed with grade C or D COPD according to the GOLD Guidelines Revised 2011 who had smoked for at least 10 pack years and who were receiving inhaled combined therapy for their COPD. The inhaled combined therapy (corticosteroid / LABA/ICS) treatment was initiated at least 1 month before entering in the study.

Evaluations:

Primary variables of the study is the total CDLM score as well as the physician evaluation of patient's general health status visual scale.

At Visit 1, each enrolled subject instructed how to complete the questionnaires, completed the first CDLM questionnaire during this office visit (referred to as baseline information), and received the questionnaires that he/she will have to complete by the next study visit.

Subjects were instructed to fill in the CDLM questionnaires at a specific time moment, around noon. In the interval between study visits, the patient complete the CDLM questionnaire in only 7 consecutive days per month, specifically in weeks 4, 8 and 12 of study period.

In order to complete the self-administered CDLM questionnaires, the patients are required to:

1) Report on their ability to carry out six different morning activities and

2) Rank the difficulty of performing each of these activities on a five-point Likert-type scale ranging from 0 (not at all difficult) to 4 (extremely difficult).

There is no weighting of the different morning activities; the total CDLM score was calculated as the average of all morning activities. Total CDLM score was calculated by study statistician, according to CDLM scoring instructions.

The total daily walking steps were registered using paedometers. In days when completed CDLM, each morning, the subject reset the device by pressing the on/reset button, attached it to the belt or pocket and at the end of the recorded the number of daily walking steps in the daily activities monitoring calendar. The study aims to evaluate the dynamics of walking distance during the study period, expressed as number of walking steps.

Demographic patient characteristics, unscheduled visits and patient adherence to treatment were also evaluated.

Statistical Methods:
This study evaluated the potential positive correlation between improvement perceived by the patient (as measured by the CDLM total score) and improvement observed by the treating physician (as measured by the patient general health status score), using the bivariate correlation test.
The statistical analysis was mainly descriptive. If statistical tests were used, they were performed 2-sided on a 5% level. No adjustment for multiple testing was done. Appropriate methods were used to derive confidence intervals, depending on the nature of the data and distribution.
Continuous data were described by their mean, standard deviation (SD), median, lower and upper quartile, minimum and maximum and valid cases. Categorical data were described by absolute and percentage number of subjects per category.
The All Subjects population was defined as all enrolled subjects.
The Full Analysis Set (FAS) is defined as all enrolled and eligible subjects.
The Per-Protocol Population (PP) is defined as all enrolled and eligible subjects who had non-missing primary variables up to Visit 4.
The FAS was used for all tables except the primary variables tables where PP was used.

RESULTS:

Subject Disposition and Demography: Subject Disposition data was summarized using absolute counts (n) and percentages (%). Percentages were based on the number of subjects with data. The descriptive statistics were used for the patient number of different visits and the patient number signed the informed consent.

Subject demographics were assessed in a descriptive manner for the analysis population.

A total of 494 subjects participated in the study. Overall, 458 subjects (92.7%) completed the study (i.e., attended Visit 4

The majority of subjects were male (365 subjects, 73.9%) and a total of 129 subjects were female (26.1%). The average age of the subjects was 66 years (range: 40 to 86 years;). Mean height at baseline was 170 cm (range: 140 to 193 cm;) and mean body weight was 78.5 kg (range: 45 to 150 kg). Mean BMI at baseline was 27.05 kg/m2 (range 15.73 to 48.44 kg/m2;).

The majority of subjects (63.4%) self-reported as ex-smokers, with the remainder being largely current smokers (35.4%). A small number of subjects (1.2%;) were reported as unknown as regards to their current smoking status.

Among subject who smoked, the mean was 1 pack (20 cigarettes) per day. The maximum number of cigarettes per day was 80. This correlated to a mean number of pack years of 32.26.

The average duration of COPD was 6.36 years, ranging from 0 to 35 years.

Overall, the majority of subjects were in group C (345 subjects, 69.8%); a total of 149 subjects were in group D (30.2%).

Nearly all of the subjects (494, 98.0%) had experienced at least 1 exacerbation of their COPD within the previous 12 months. The mean number of exacerbations was 2.08.

Treatment and Dosing:

With regards to COPD medications, the majority of subjects (61.5%) were using budesonide/formoterol, while 37.2% were taking salmeterol/fluticasone and a small number of subjects: 1.2% of the population. The mean duration of combined inhaled therapy was 47.07 months (range: 0.2 to 153 months). Only data for the most recent combined inhalation therapy for each subject was included.

Among the other COPD medications (i.e., not combined inhaled therapy) the most frequently reported was Long acting anticholinergic for 298 subjects (60.3%).

Results:

The correlation between the CDLM total score and the 5-scale general health status score was investigated at every visit using the Kendall tau-b correlation test (Table 11). A significant positive correlation was identified on every visit, with a range from *0.3197* to *0.3922* of Kendall tau-b values, implying a moderate positive connection between the 2 parameters.

Secondary objectives are analysed in the FAS population (N=494 subjects). However, CDLM and health status, adherence to treatment changes, and p-values between visits are calculated within the PP population (N=193). In the FAS analysis, at Visit 1, the mean CDLM score was 3.74, increasing to 3.89 at Visit 4. A number of subjects at each visit had incomplete CDLM data, resulting in a smaller n for CDLM total score calculations than implied by the FAS group criteria.

In the PP population analysis, at Visit 1, the mean CDLM score was 3.85, increasing to 3.89 at Visit 4.

The general health status for the patients was indicated using a scale of 5 levels (1= very bad, 5= very good) as evaluated by the investigators at each visit.

For the FAS analysis, at Visit 1, 36% of patients had a score of 4/5. The proportion increased at each visit, and reached 53.1% at Visit 4.

Results were similar for the PP population analysis, with the percentage of patients with a score of 4/5 of 39.9% at Visit 1, increasing to 55.4% at Visit 4.

The improvement in health status improvement from Visit 1 to Visit 4 was significant (based on the Wilcoxon signed rank test).

Patients used a pedometer to measure their daily walking distance on 7 consecutive days between the visits. The mean of the daily averages of number of steps on Visit 2 was 2473.62 and decreased to 2355.62 on Visit 4.

The difference of daily averages of number of steps between the visits was significant (based on Wilcoxon signed rank test).

Results for the PP group for both effort tolerance and change in effort tolerance were similar to those experienced in the study group as a whole. The mean of the daily averages of number of steps on Visit 2 was 2616.14, and decreased to 2478.99 on Visit 4. The difference of daily averages of number of steps between the visits 2&3 and 3&4 were significant (p-values of 0.0027 and 0.0149 respectively), but was not significant between visits 2&4 (p-value 0.1833).

The change in incidence and impact of COPD exacerbations was small, with the percentage of subjects with exacerbations ranging from 3.4% to 4.1% across all visits. Less than 1% of subjects reported to the ER for COPD exacerbations, ≤1.1% of subjects required hospitalization because of a COPD exacerbation, and less than 1% of subjects visited a physician due to a COPD exacerbation.