AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: N/A
ACTIVE INGREDIENT: Non-drug study

Study No: D9612L00096
A Cluster-Randomized Study to Examine National Characteristics and Outcome Measures of GERD patients utilizing the PPI Acid Suppression Symptom (PASS) test for response [EncomPASS]

Developmental phase: IV
Study Completion Date: Last Subject Out: March 22, 2007
Date of Report: N/A

OBJECTIVES:

Primary:

To compare the improvement in burden of overall GERD symptoms after 4 weeks of treatment with Nexium® versus maintenance of current therapy in subjects with persistent GERD symptoms.

Secondary:

To examine the relationship of the severity and frequency of GERD symptoms to treatment, at national and regional levels.

To document the characteristics of gastroesophageal reflux disease and the management of the disease.

To identify factors, including symptoms, which predict a likelihood of response or non-response to Nexium®, for subjects with incomplete response to current therapy, as determined by the PASS test.

To evaluate the performance of the PASS tool in the broad spectrum of GERD subjects.

To measure subject adherence and treatment satisfaction with a prescription over a 4-week period.

METHODS:

Study Design and Patients

- This was a multicentre, cluster-randomised, open-label study in adults with GERD who were enrolled at primary care centres across Canada. Centres were randomised on a 1:1 ratio to either an intervention ('I') group or a control-intervention ('C') group.

- GERD symptom control at baseline was assessed using the PASS test. Eligible subjects who failed the PASS test (ie, answered 'yes' to one or more questions) received esomeprazole 20 mg or 40 mg once daily ('I' centres; dose according to physician discretion), or continued on their current therapy for a period of 4 weeks ('C' centres). *Note the patients were not provided with study medication*. Subjects enrolled at 'C' centres who failed a further PASS test at Week 4 were assigned to a further 4 weeks of treatment with esomeprazole 20 mg or 40 mg once daily.

- The primary variable was the change in Global Overall Symptom (GOS) score from baseline until Week 4 [the GOS score is a previously validated subject self-assessment test in which the severity of dyspepsia symptoms is graded on a 7-point scale]. Secondary variables included: PASS test score, Reflux Disease Questionnaire (RDQ) domain scores, and Quality of Life in Reflux and Dyspepsia (QOLRAD) questionnaire domain scores at Week 4. The primary and secondary variables were also recorded at Week 8 for 'C' intervention patients who failed the PASS test at Week 4 and were switched to esomeprazole.

- In addition, standard safety and tolerability assessments were performed.

RESULTS:

- The intention-to-treat population comprised 1564 patients (43% men). Some 973 patients (650 on prior PPIs) were recruited at 136 'I' centres and 591 (362 on prior PPIs) at 92 'C' centres. *Summary of patient characteristics* (Table 1) *and flow of patients through the study* (Figure 2).

- The majority of patients (96%) under the care of 'I' centres received esomeprazole 40 mg once daily.

<u>Global Overall Symptom score</u>

- *Summary of GOS scores at baseline and Week 4, and change from baseline* (Table 2).

    - The difference in change in GOS scores from baseline until Week 4 between the treatment arms was -0.9 (95% CI: -1.1 to -0.6; $p<0.0001$) for ITT patients, and -0.8 (-1.1 to -0.6; $p<0.0001$) for patients on PPIs at baseline.

    - GOS symptom relief (ie, 'no problem') was achieved by 69.0% (563/816) of 'I' patients 'compared with 37.4% (170/454) of 'C' patients ($p<0.0001$). *Findings for those on prior PPI treatment*.

- Improvements in GOS score (-1.3; $p<0.0001$) were also observed in patients treated at 'C' centres who were switched to esomeprazole at Week 4, including those who were taking PPIs at baseline (-1.3; $p<0.001$).

<u>PASS test</u>

- At Week 4, 35.5% of 'I' patients (345/973) achieved a positive PASS test compared with 13.2% of 'C' patients (78/591) ($p<0.0001$).

RDQ and QOLRAD

- *Summary of RDQ scores at baseline and Week 4, and change from baseline* (Table 3).
    - Significant difference in favour of 'I' treatment for all domains (including frequency and severity of heartburn) and overall score.
    - Comparison of RDQ (asymptomatic) between treatments at Week 4.
- *Summary of QOLRAD scores at baseline and Week 4, and change from baseline* (Table 4).
    - Significant difference in favour of 'I' treatment for all domains.
- Similar improvements in RDQ/QOLRAD domains were apparent for 'C' PASS test failures switched to esomeprazole at Week 4.