STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Nexium®
ACTIVE INGREDIENT: Esomeprazole

Study No: IMPACT; NCT00524251; Study Code N11
IMPACT: Impact of Gastro-intestinal complaints in Patients without Acid Control Therapy

Developmental phase: Non Interventional Study (Phase IV)
Study Completion Date: Database lock 13 March 2008
Date of Report: February 2009

OBJECTIVES:

Primary objective:

- Determine whether the improvement in quality of life after start of esomeprazole treatment is the same for patients who have made lifestyle adjustments as it is for patients who have not made any lifestyle adjustments prior to the start of treatment (baseline).

Secondary objectives:

- Evaluation of the quality of life measured at baseline in relation to lifestyle changes
- Determination of the improvement in the quality of life in all patients after start of esomeprazole treatment compared to quality of life at baseline.
- Determination of the frequency and nature of the lifestyle adjustments made prior to consulting a physician for the reflux disease.
- Evaluation of the motives of the reflux patients to consult a physician.

METHODS:

The study was an observational study without intervention in the treatment strategy of the patient. Patients eligible for the study were patients with reflux complaints for whom therapy with esomeprazole 40 mg once daily was prescribed by their general practitioner. Patients that used a PPI or a H_2-RA on prescription in the month prior to the start of the study were not eligible for participation in the study. Consult 1 took place when the physician had decided to start treatment with esomeprazole (baseline). Consult 2 took place after 2 weeks (or more) of esomeprazole treatment. Quality of Life was measured with The QOLRAD questionnaire (Quality of Life in Reflux and Dyspepsia Patients). The questionnaire consists of 25 questions and addresses 5 dimensions that are of importance in the daily functioning of a reflux patient: physical/social functioning, sleeping disorders, emotion, vitality and eating/drinking disorders. It was expected that the difference in mean change in QOLRAD score between the two groups is smaller than the minimal clinically significant difference of 0.5. This was tested by two one-sided procedure at 5% level of significance each.

Table 1: Study assessments by consult

	Consult 1	Consult 2
	Baseline	after esomeprazole treatment for 2 weeks or more
Demographics	X	
Inclusion criteria	X	
Reasons for consultation	X	
Other reflux medication	X	
Esomeprazole prescription	X	
Lifestyle adjustments	X	X
QOLRAD questionnaire for patients with reflux complaints	X	X
esomeprazole usage in past week		X
Adverse events leading to discontinuation		X
Serious Adverse events		X

RESULTS:

A total of 637 patients from 91 centers were included in this study. Of these patients, 632 were included in the ITT population and 625 could be used for the efficacy evaluation. For most patients (82,8%), esomeprazole was prescribed for two weeks. Almost all the patients, (92%) had used the drug daily in the week before the second consult.

For the total group (n=625), the overall QOLRAD score increased after treatment with esomeprazole (baseline score: 4,0 vs score at visit 2: 5,7). At Consult 1, the QOLRAD score differed significantly between the two lifestyle groups (3.8 vs 4.3; p<0.0001) (Table 2). After treatment with 40 mg esomeprazole, the increase in the group with lifestyle adjustments was significantly higher (p=0.0037) than in the group without lifestyle adjustments. For both groups and overall, the increase in QOLRAD scores after treatment with esomeprazole was significant (all p <0.0001). Although the group without lifestyle adjustments showed a significant lower increase (difference: 0.3), this difference and corresponding 90% CI (-0.4 to -0.1) are between the clinical significant limits of -0.5 to 0.5.

Table 2: QOLRAD scores for groups with and without lifestyle changes

	With lifestyle adjustments			Without lifestyle adjustments				
	N	Mean	SD	n	Mean	SD	Difference**	90% CI
Consult 1	413	3.8	1.0	212	4.3	1.2	0.4	0.3 - 0.6
Consult 2	413	5.7	1.0	212	5.8	1.1	0.1	0.0 - 0.3
Difference*	413	1.9	1.1	212	1.6	1.2	-0.3	-0.4 - -0.1

SD = standard deviation; CI = Confidence interval; n = number of patients with data available; * Mean of the individual differences between consult 2 and consult 1. ** Difference between the 2 groups

The scores for the subcategories in QOLRAD scores show the same pattern as the overall mean QOLRAD scores. Mean overall increases in QOLRAD scores were: 1.5 for physical/social functioning, 1.8 for sleep dysfunction, 1.7 for emotional distress, 1.8 for vitality and 2.0 for food/drink problems. The differences in increase of QOLRAD score after esomeprazole treatment between the groups with and without lifestyle adjustments are within the clinical significant limits for each subcategory.

Sixty percent (60%) of the patients did not use concomitant medication for reflux disease at baseline. Sixty-five percent (65%) of the patients in the ITT population made lifestyle adjustments prior to consult 1 (table 3). Patients using concomitant medication and females seemed to make lifestyle adjustments more often (78% concomitant medication vs 58% no concomitant medication; 70% female vs 61% male). Patients in the youngest age group less often made lifestyle adjustments (57%) and used concomitant medication less often (82% no concomitant medication).

Table 3: Lifestyle adjustments

	Adjustments before consult1 (N=632) n (%)	Adjustments mentioned at consult 2 (N=627) n(%)
None	215 (34.0)	183 (29.2)
Stop smoking	91 (14.4)	89 (14.2)
Avoid alcohol	145 (22.9)	158 (25.2)
Dietary changes	325 (51.4)	351 (56.0)
Deliberate weight loss when overweight	74 (11.7)	91 (14.5)
Raise head of the bed because of nocturnal complaints	99 (15.7)	140 (22.3)
Other	30 (4.7)	15 (2.4)
MISSING		3 (0.5)

n=number of patients with data available; Percentage calculation based on ITT

Reasons for visiting the GP are depicted in table 4:

Table 4: Reason for GP visit

Reason for visit		
Seeks solutions for complaints	n (%)	502 (79.4)
Fear/concern that complaints are related to a Serious condition	n (%)	167 (26.4)
Person in direct environment is worried	n (%)	62 (9.8)
Freely available medication (OTC) from chemist/Pharmacy does not work/works insufficiently	n (%)	102 (16.1)
Complaints have negative impact on social life/work	n (%)	153 (24.2)
Nocturnal complaints disturb sleep	n (%)	143 (22.6)
Other	n (%)	18 (2.8)

n = number of patients with data available; Calculation of percentages based on ITT

Adverse events leading to discontinuation of the study drug were reported in 3 patients (0.5 % of total patients). Two of these events included perceived ineffectiveness of the study drug. No serious adverse events were observed.