

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: None

ACTIVE INGREDIENT: None

Study No: NIS-GEU-DUM-2008/1 (NCT00842387)

Evaluation Study of a Management Strategy for Gastroesophageal Reflux Disease (GERD)

Developmental phase: Epidemiological Study

Study Completion Date: 17 Dec 2009 (Last subject last visit)

Date of Report: 02 Dec 2010

OBJECTIVES:

1) Primary objective:

To compare the clinical outcome (control of symptoms of GERD) in patients treated at PCCs where the structured pathway was implemented with the clinical outcome of those treated at centres without this implementation. The clinical control of the disease will be based on:

- a) Results of GerdQ.
- b) Percentage of patients who need a different treatment as a result of therapy failure (no significant improvement, no disappearance of symptoms) of the drug initially prescribed and taken for the first four weeks.
- c) Percentage of patients requiring referral to a specialist after having being treated for a maximum of 8 weeks.

2) Secondary objectives:

- 2.1. To describe the rate of adoption of the clinical pathway by physicians working in PCCs participating in the study and in which the pathway has been implemented.
- 2.2. To explain how certain intrinsic characteristics of the physician/PCC may affect the rate of adoption of a new clinical pathway.
- 2.3. To compare the use of resources during the study between centres where the structured pathway has been implemented and those where it has not.

METHODS:

Five cluster-randomised prospective studies that were conducted at multiple study centres in Austria, Italy, Norway, Spain and Sweden were integrated in the GMP to compare a new structured treatment pathway for primary care patients with GERD with existing treatment practice to determine whether clinical outcomes are improved.

The use of a standard study protocol with regional modifications enabled regional guidelines and regulatory requirements to be met. Demographic and clinical information was collected for both patient groups (structured versus standard treatment). Efficacy data were collected after 4 weeks' follow-up. Patients who had not improved sufficiently at 4 weeks were reassessed at 8 weeks.

The structured treatment pathway was based on the self-administered GerdQ to identify patients with a high probability of being a GERD patient (GerdQ score ≥ 8). Within this group patients who had an impact score of ≤ 2 (≤ 3 in Norway) were classified as the low/moderate impact GERD group and treated with generic proton pump inhibitors according to local guidance; patients with an impact score of ≥ 3 (≥ 4 in Norway) were classified as the high impact GERD group and treated with esomeprazole 40 mg once daily.

Treatment response was determined by the GerdQ score and defined as patients scoring < 2 for the items of heartburn, regurgitation, need for OTC treatment, sleep disturbance (on at most 1 day during the previous 7 days).

The study outcomes were the change in GerdQ score and the proportion of participants with a GerdQ ≥ 8 at the follow-up visit.

Adult (aged ≥ 18 years) male and female primary care patients with symptoms suggestive of GERD were recruited into the studies.

Differences in baseline characteristics of study patients by treatment group were calculated using t-tests or χ^2 tests, as appropriate. The study outcomes, defined a priori, were the change in GerdQ score (follow-up – baseline) and the proportion of participants with a GerdQ ≥ 8 at the follow-up visit. The change in GerdQ score comparing the treatment and the implementation groups was estimated using mixed linear models with random intercepts to take clustering by study center (clinic) into account. All analyses were stratified by country and adjusted by baseline GerdQ scores. In addition, we also estimated the treatment effect in a model further adjusted by age (continuous), sex, smoking (current vs. non-current), and alcohol intake (current vs. non-current).

To compare the proportion of participants with GerdQ scores ≥ 8 at the follow-up visit in the implementation vs. the control groups, we used mixed logistic models with random intercepts to take clustering by study center (clinic) into account. Odds ratios for follow-up GerdQ ≥ 8 comparing the implementation vs. control groups were estimated in models stratified for center and adjusted for baseline GerdQ score, and then in models further adjusted by age (continuous), sex, smoking (current vs. non-current), and alcohol intake (current vs. non-current).

Subgroup effects by country, age (< 60 and ≥ 60 years), sex, smoking (current and non-current), and alcohol intake (current and non-current) were estimated by introducing product terms of study variables in fully adjusted mixed linear or logistic models, as appropriate. P-values for the interactions were obtained by testing for the statistical significance of these product terms. All P-values reported were 2-sided. Results were considered statistically significant if the 2-sided P-value was < 0.05 . Statistical analyses were conducted using STATA, version 11 (StataCorp, College Station, TX).

RESULTS:

Table 1. Patients' baseline characteristics

	Treatment group		P-value
	Structured treatment	Standard regional treatment	
Country			
Austria	277 (33.2)	308 (34.2)	
Italy	164 (19.7)	171 (19.0)	
Norway	170 (20.4)	165 (18.3)	
Spain	153 (18.4)	128 (14.2)	
Sweden	70 (8.4)	128 (14.2)	
Age, years	52.6 (15.0)	54.2 (15.4)	0.03
Sex, male	427 (47.4)	386 (46.3)	0.63
Current smokers	235 (26.1)	233 (27.9)	0.39
Current drinkers	343 (38.1)	276 (33.1)	0.03
Date of diagnosis*			0.49
Before 2009	349 (55.5)	281 (53.6)	
2009	277 (44.3)	243 (46.4)	

All values are n (%), except for age (mean [SD]).

* Based on 1149 patients with available date of diagnosis

Table 2. Summary of patient baseline characteristics, by country

	Austria		Italy		Norway		Spain		Sweden	
	Structured treatment (n=277)	Standard treatment (n=308)	Structured treatment (n=164)	Standard treatment (n=171)	Structured treatment (n=170)	Standard treatment (n=165)	Structured treatment (n=153)	Standard treatment (n=128)	Structured treatment (n=70)	Standard treatment (n=128)
Age, years	57.8 (14.9)	55.5 (15.6)	52.9 (14.2)	50.8 (14.4)	50.1 (15.3)	47.5 (14.7)	50.2 (15.0)	51.0 (13.6)	61.9 (14.6)	56.4 (14.0) ^a
Sex, male	136 (49.1)	164 (53.3)	73 (44.5)	71 (41.5)	86 (50.6)	90 (54.6)	69 (45.1)	46 (35.9)	22 (31.4)	56 (43.8)
Current smokers	104 (37.6)	117 (38.0)	32 (19.5)	36 (21.1)	46 (27.1)	37 (22.4)	42 (27.5)	27 (21.1)	9 (12.9)	18 (14.1)
Current drinkers	38 (13.7)	57 (18.5)	62 (37.8)	60 (35.1)	120 (70.6)	121 (73.3)	10 (6.5)	4 (3.1)	46 (65.7)	101 (78.9) ^b
Diagnosis in 2009*	25 (20.3)	18 (11.3) ^b	66 (40.2)	64 (37.4)	55 (74.3)	108 (85.7) ^b	95 (62.1)	85 (66.4)	2 (20.0)	2 (4.9)

^a p<0.01 vs structured treatment group; ^b p<0.05 vs structured treatment group.

* Date of diagnosis was available in 1149 patients.

Table 3. GerdQ scores by country and treatment group.

	Treatment group	
	Control	Implementation
Austria		
Number of patients	308	277
Baseline	9.80 (3.77)	10.65 (2.97)
Follow-up	3.60 (3.20)	3.08 (2.61)
Change follow-up - baseline	-6.20 (4.02)	-7.57 (4.18)
Italy		
Number of patients	171	164
Baseline	9.12 (4.22)	7.51 (3.22)
Follow-up	4.25 (3.84)	2.33 (2.75)
Change follow-up - baseline	-4.88 (4.74)	-5.18 (3.61)
Norway		
Number of patients	165	170
Baseline	8.24 (3.59)	8.41 (3.40)
Follow-up	3.16 (3.43)	2.64 (3.26)
Change follow-up - baseline	-5.08 (4.03)	-5.77 (4.25)
Spain		
Number of patients	128	153
Baseline	9.84 (2.78)	11.17 (2.66)
Follow-up	7.65 (2.13)	7.35 (2.17)
Change follow-up - baseline	-2.20 (3.16)	-3.82 (3.11)
Sweden		
Number of patients	128	70
Baseline	7.54 (4.02)	8.67 (3.71)
Follow-up	5.09 (4.09)	3.41 (3.49)
Change follow-up - baseline	-2.45 (4.54)	-5.26 (4.08)
OVERALL		
Number of patients	900	834
Baseline	9.07 (3.83)	9.50 (3.43)
Follow-up	4.43 (3.67)	3.65 (3.31)
Change follow-up - baseline	-4.64 (4.41)	-5.85 (4.12)

Values in the Table are mean (SD).

Table 4. Efficacy of intervention vs. control in changing GerdQ scores.

	Average difference in GerdQ score change Implementation – Control			
	N	Efficacy	(95% CI)	P-value heterogeneity
Overall*	1,734	-0.75	(-1.10 to -0.40)	—
Overall	1,734	-0.74	(-1.10 to -0.39)	—
Country				0.20
Austria	585	-0.55	(-1.15 to 0.04)	
Italy	335	-1.52	(-2.43 to -0.62)	
Norway	335	-0.56	(-1.18 to 0.06)	
Spain	281	-0.40	(-1.37 to 0.56)	
Sweden	198	-1.96	(-3.68 to -0.25)	
Age				0.89
<60 years	1,131	-0.77	(-1.18 to 0.37)	
≥60 years	603	-0.73	(-1.26 to -0.20)	
Sex				0.42
Men	813	-0.62	(-1.08 to -0.17)	
Women	921	-0.85	(-1.30 to -0.41)	
Current smokers				0.16
No	1,266	-0.61	(-1.01 to -0.21)	
Yes	468	-1.06	(-1.65 to -0.49)	
Current drinkers				0.90
No	1,115	-0.76	(-1.18 to -0.33)	
Yes	619	-0.72	(-1.24 to -0.19)	
Date of diagnosis**				0.05
Before 2009	629	-1.50	(-2.03 to -0.97)	
2009	520	-0.80	(-1.36 to -0.24)	

Results in the Table were estimated from mixed linear models with random intercepts for study center (clinic). A negative estimate indicates that the implementation group was superior to the control group in reducing GerdQ scores.

* Stratified by country and adjusted for baseline GerdQ score. All other analyses were further adjusted for age, sex, smoking, and alcohol intake.

** Based on N = 1,149 patients with available date of diagnosis.

Table 5. Number (proportion) of participants with GerdQ scores ≥ 8 by country and treatment group.

	Treatment group	
	Control	Implementation
Austria		
Total number of patients	308	277
Number of patients with GerdQ ≥ 8		
Baseline	221 (71.8)	243 (87.7)
Follow-up	39 (12.7)	19 (6.9)
Italy		
Total number of patients	171	164
Number of patients with GerdQ ≥ 8		
Baseline	105 (61.4)	85 (51.8)
Follow-up	34 (19.9)	10 (6.10)
Norway		
Total number of patients	165	170
Number of patients with GerdQ ≥ 8		
Baseline	99 (60.0)	100 (58.8)
Follow-up	21 (12.7)	16 (9.4)
Spain		
Total number of patients	128	153
Number of patients with GerdQ ≥ 8		
Baseline	102 (79.7)	142 (92.8)
Follow-up	56 (43.8)	53 (34.6)
Sweden		
Total number of patients	128	70
Number of patients with GerdQ ≥ 8		
Baseline	60 (46.9)	46 (65.7)
Follow-up	34 (26.6)	12 (17.1)
OVERALL		
Total number of patients	900	834
Number of patients with GerdQ ≥ 8		
Baseline	587 (65.2)	616 (73.9)
Follow-up	184 (20.4)	110 (13.2)

Values in the Table are number of patients (%).

Table 6. Odds ratios for GerdQ score ≥ 8 at follow-up comparing intervention vs. control groups.

Odds ratios for GerdQ score ≥ 8 at follow-up Implementation vs. Control				
	N	Odds ratio	(95% CI)	P-value heterogeneity
Overall*	1,734	0.53	(0.36 to 0.78)	—
Overall	1,734	0.53	(0.36 to 0.78)	—
Country				0.68
Austria	585	0.50	(0.24 to 1.03)	
Italy	335	0.31	(0.11 to 0.85)	
Norway	335	0.71	(0.34 to 1.48)	
Spain	281	0.67	(0.29 to 1.53)	
Sweden	198	0.35	(0.07 to 1.69)	
Age				0.56
<60 years	1,131	0.56	(0.36 to 0.87)	
≥ 60 years	603	0.46	(0.26 to 0.83)	
Sex				0.91
Men	813	0.54	(0.32 to 0.91)	
Women	921	0.52	(0.33 to 0.83)	
Current smokers				0.39
No	1,266	0.58	(0.38 to 0.90)	
Yes	468	0.43	(0.23 to 0.80)	
Current drinkers				0.90
No	1,115	0.52	(0.33 to 0.82)	
Yes	619	0.55	(0.30 to 1.01)	
Date of diagnosis				0.09
Before 2009	629	0.27	(0.15 to 0.50)	
2009	520	0.55	(0.28 to 1.07)	

Results in the Table were estimated from mixed logistic models with random intercepts for study center (clinic). Odds ratios less than 1 indicates that the implementation group had a lower proportion of participants with GerdQ score ≥ 8 at the follow-up visit.

* Stratified by country and adjusted for baseline GerdQ score. All other analyses were further adjusted for age, sex, smoking, and alcohol intake.

** Based on N = 1,149 patients with available date of diagnosis.