

Cost Analysis of Long-Term Treatment of Patients with Symptomatic Gastroesophageal Reflux Disease (GERD) with Esomeprazole On-Demand Treatment or Esomeprazole Continuous Treatment: An Open, Randomized, Multicenter Study in Switzerland*

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[Correction added after online publication 23-September-2008: The footnotes for Table 7 have been updated]

ABSTRACT

Objectives: To assess the difference in direct medical costs between on-demand (OD) treatment with esomeprazole (E) 20 mg and continuous (C) treatment with E 20 mg q.d. from a clinical practice view in patients with gastroesophageal reflux disease (GERD) symptoms.

Methods: This open, randomized study (ONE: on-demand Nexium evaluation) compared two long-term management options with E 20 mg in endoscopically uninvestigated patients seeking primary care for GERD symptoms who demonstrated complete relief of symptoms after an initial treatment of 4 weeks with E 40 mg. Data on consumed quantities of all cost items were collected in the study, while data on prices during the time of study were collected separately. The analysis was done from a societal perspective.

Results: Forty-nine percent (484 of 991) of patients randomized to the OD regimen and 46% (420 of 913) of the patients in the C group had at

least one contact with the investigator that would have occurred nonprotocol-driven. The difference of the adjusted mean direct medical costs between the treatment groups was CHF 88.72 (95% confidence interval: CHF 41.34–153.95) in favor of the OD treatment strategy (Wilcoxon rank-sum test: $P < 0.0001$). Adjusted direct nonmedical costs and productivity loss were similar in both groups.

Conclusions: The adjusted direct medical costs of a 6-month OD treatment with esomeprazole 20 mg in uninvestigated patients with symptoms of GERD were significantly lower compared with a continuous treatment with E 20 mg once a day. The OD therapy represents a cost-saving alternative to the continuous treatment strategy with E.

Keywords: cost-effectiveness, costs, economic evaluation, esomeprazole, gastroesophageal reflux disease, proton pump inhibitor.

Introduction

Reflux disease is a growing public health problem. Not only does this condition cause multiple clinical problems, it is also associated with a large economic burden.

In Switzerland, the prevalence of reflux disease in Swiss adults was estimated at 17.6% (95% confidence interval [CI] 15.6–19.7%) or 993,000 individuals [3]. The disease was more frequent in the French-speaking part of the country and rising with age, while being equally distributed among the sexes. Regular treatment with medication was reported by 38.0% of the individuals with gastroesophageal reflux disease (GERD) symptoms. Reflux-induced general practitioner office visits during the last year were reported by 25.9%. On average, there were 0.84 general practitioner consultations, 0.19 specialist consultations, and 0.01 hospitalizations annually. Mean direct medical costs, dominated by medication costs, were CHF 185 per patient-year (95% CI CHF 140–230) or CHF 0.18 billion per year in Switzerland. Total costs amounted to CHF 234 (95% CI CHF 185–284), thus the total costs of reflux disease in Switzerland amounted to CHF 0.23

billion per year. In consequence, the direct medical costs of reflux disease accounted for approximately 0.5% of the total Swiss health-care expenditures.

Esomeprazole, the S-enantiomere of omeprazole, is a proton pump inhibitor that produced an increased duration and level of inhibition of gastric acid secretion than pantoprazole, lansoprazole, rabeprazole and omeprazole in different studies [4–6]. Patients treated with esomeprazole experienced a rapid relief of their GERD symptoms [7–10]. Because of stronger acid suppression, esomeprazole is a promising drug for patient-driven treatment (i.e., on-demand treatment, according to the patient's own judgment).

In clinical practice, patients with GERD symptoms are often treated empirically with proton pump inhibitors without investigation by, for example, endoscopy. When the patient is free from GERD symptoms, there are two main options available to the treating physician for the long-term management of the disease. The physician can prescribe continuous daily treatment or on-demand treatment as required to control symptoms.

Given the advent of highly efficacious medications and trends suggesting an increase in disease prevalence and incidence, it is necessary to appraise the costs and the consequences of GERD treatment. Most importantly, it is yet unknown what the economic difference is between a long-term maintenance treatment strategy and an on-demand treatment strategy. The present publication focuses on the comparison of the two treatment options concerning health economic aspects.

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Economic Study Perspective

The types of costs that should be included in an economic evaluation depend on the perspective adopted [11]. It is generally recommended that a societal perspective should be adopted, and that all types of costs should be included. First, there are direct costs, which occur as a result of changes in health-care utilization because of an intervention. Direct costs can be divided into medical, such as costs borne by the health-care provider (e.g., drugs, health-care visits, tests), and nonmedical, such as costs borne by the patient (e.g., transport to visits, housekeeping, home modifications). Second, there are indirect costs, which are costs for changes in productivity owing to morbidity and mortality. Examples of typical indirect costs are loss of production because of absenteeism from work and early retirement.

Objectives

The primary objective of this prospective health economic study was to assess the difference in direct medical costs between on-demand treatment with esomeprazole 20 mg and continuous treatment with esomeprazole 20 mg q.d. from a clinical practice view in patients with GERD symptoms.

The secondary objectives were to measure direct nonmedical costs and indirect costs during the maintenance phase, to measure patient satisfaction with treatment strategy, to assess time to first relapse, defined as time to the patient's contact to the investigator because of need for change of treatment because of insufficient control of symptoms, and to assess symptoms at each study visit.

Methods

We conducted an open-label, randomized, multicenter study (ONE: on-demand Nexium [AstraZeneca, London, UK] evaluation) comparing the two long-term management options with esomeprazole 20 mg—continuous daily or on-demand treatment during 26 weeks—in endoscopically uninvestigated patients seeking primary care in Switzerland for symptoms suggestive of GERD who demonstrated complete relief of symptoms after an initial treatment of 4 weeks with esomeprazole 40 mg.

The study was intended to be naturalistic in accordance with health economic methodology while still maintaining control of events where possible. An open study design is in accordance with treatment in clinical practice, where both the treating physician and the patient are aware of the treatment regimen. Costs were assessed during the whole maintenance phase, including costs following an endoscopy, as well as costs because of a patient or investigator-driven decision that the patient should no longer abide with the study therapy.

Male and female patients (≥ 18 years of age) seeking primary care for symptoms suggestive of GERD (heartburn as the predominant symptom with or without acid regurgitation; for 3 days or more during the last 7 days), were enrolled into the study and had an initial treatment course for 4 weeks with esomeprazole 40 mg q.d. after having given written informed consent.

The main exclusion criteria were as follows: Existence of any significant "alarm symptoms," such as unintentional weight loss, gastrointestinal bleeding, dysphagia, jaundice, or any other sign indicating serious or malignant disease. Patients with known history of complications of GERD, such as Barrett's esophagus, esophageal stricture, ulcer, or significant dysplastic changes in the esophagus and or a history of esophageal, gastric, or duodenal surgery were excluded. Excluded from the study were patients with current or historical evidence of irritable bowel syndrome, Zollinger-Ellison syndrome, primary

esophageal motility disorder(s), gastric or duodenal ulcers within the last 3 months, malabsorption, unstable diabetes mellitus, or cerebrovascular disease. Patients in need for continuous concurrent therapy of diazepam, phenytoin, or warfarin were also excluded. Pregnancy and lactation were also exclusion criteria. After this initial 4-week treatment course with esomeprazole 40 mg, the asymptomatic patients (defined as patients with complete resolution of symptoms of not more than 1 day, with mild symptoms during the last 7 days before the visit) continued with the study. Patients with persistent symptoms after 4 weeks left the study and were treated according to routine clinical procedures.

Patients found to meet all the inclusion criteria and none of the exclusion criteria at the end of the initial treatment course were randomized in equal proportions to continuous treatment with esomeprazole 20 mg q.d. or on-demand treatment with esomeprazole 20 mg. For the randomization, a centrally compiled, computer-generated list was used, which was based on a block size of four. Each site received a kit consisting of a list of randomization numbers and sealed randomization envelopes for four patients. The investigator was instructed to consecutively allocate the lowest available randomization number, but open the randomization envelopes containing the information on the allocated treatment group only at randomization. It had been planned that each site would recruit four patients (or an exact multiple of four).

Each patient in the continuous treatment arm was instructed to take one tablet once daily. In the on-demand arm, the patient was instructed to take one tablet daily if needed for the relief of heartburn and to stop when the heartburn is adequately controlled. The study drugs were packed in bottles, and every patient received in total two bottles of 100 tablets esomeprazole 20 mg free of charge. The distribution schedule of the study drugs from general practitioner to patient was at the discretion of the general practitioner, i.e., the treating physician decided when to distribute study drugs and whether to distribute them all at once or at several occasions. Compliance was determined by counting the tablets returned by the patient.

Patients were instructed to contact the center if they experienced symptom relapse (i.e., need for change of therapy in the on-demand or continuous treatment groups). In such situations, the patients were given a 4-week treatment course with esomeprazole 40 mg q.d. supplied to the patient at unscheduled visits necessary for this event. If symptom-free at the end of this treatment course, the patients continued the long-term treatment to which they were originally allocated. Patients with persisting symptoms remained in the study, but were treated at the discretion of the investigator. Patients leaving the study prematurely at any time after randomization were followed with regard to costs for the remainder of the study. Endoscopy could be carried out at any time during the long-term treatment phase at the discretion of the investigator.

During the maintenance phase, there was a scheduled visit only at study completion, while unscheduled visits were made in accordance with treatment in clinical practice and guided by the patient's need for therapy or change of therapy. At each visit after randomization, the physician assessed whether the contact would have occurred in clinical practice. Telephone interviews with each patient to collect GERD-related information on health economic data, patient satisfaction, and symptoms were conducted every 5 to 6 weeks, resulting in three to four interviews per patient during the maintenance phase. A nonmedical but trained interviewer, who was not allowed to give any medical advice to the patient, carried out the telephone interviews by asking specific questions to collect the study information.

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