Gastrointestinal Events Among Patients Initiating Osteoporosis Therapy: A Retrospective Administrative Claims Database Analysis

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ABSTRACT

Purpose: Our purpose was to characterize the occurrence of gastrointestinal (GI) events among women on oral bisphosphonate therapy.

Methods: This was a retrospective cohort study that used a United States (US) claims database. The study period was from January 1, 2000, to December 31, 2011. The index date was the date of the first oral bisphosphonate (alendronate, ibandronate, or risedronate) prescription and occurred between January 1, 2001, and December 31, 2010. The pre- and post-index periods were the 1-year periods before and after the index date, respectively. The analysis included women with osteoporosis aged ≥55 years at the index date who were naive to all osteoporosis treatments before the index date and were continuously enrolled in the health plan for at least 1 year before and 1 year after the index date. Patients with a diagnosis of malignant neoplasm during the pre- or post-index periods or a diagnosis of Paget disease anytime in the claims history were excluded. The occurrence of GI events (defined as esophagitis; gastroesophageal reflux disease; ulcer, stricture, perforation, or hemorrhage of the esophagus; gastric, duodenal, or peptic ulcer; acute gastritis; duodenitis; GI hemorrhage; nausea/vomiting; or dysphagia) was assessed during the pre-index period and at 3, 6, and 12 months in the post-index period. The rate of GI events was defined as the percentage of patients having at least 1 GI event in each analysis period (ie, pre-index and post-index periods). GI events in the post-index period were also stratified by the presence of GI events in the pre-index period.

Findings: A total of 75,593 women were included in the analysis. The average age at the index date was 64.4 years. Gastroprotective agents were used by 17.9% of patients. Approximately one fourth of patients (26.6%; n = 20,073) had ≥1 GI events in the pre-index period. Approximately the same proportion of patients (28.0%; n = 21,142) experienced GI events in the post-index period. The cumulative rate of GI events during the post-index period was higher among patients who had GI events in the pre-index period (51.2%) than among patients without a GI event in the pre-index period (19.6%).

Implications: Among women with osteoporosis enrolled in a US commercial plan, GI events were common regardless of bisphosphonate use. Approximately one fourth of US women on bisphosphonate therapy experienced GI events within the year after initiation of therapy, and one half of US women with a previous GI event had another event while taking bisphosphonates. (*Clin Ther.* 2015;37:1228–1234)

Key words: adverse effects, bisphosphonates, drug therapy, gastrointestinal diseases, postmenopausal osteoporosis.

INTRODUCTION

Approximately 15% of women in the United States (US) aged ≥50 years have osteoporosis,[1,2] a skeletal disease characterized by loss of bone density and associated with an increased risk of fracture.[3,4] An

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estimated 30% of women in this age range have a high enough risk of osteoporotic fracture to be considered eligible for pharmacologic treatment.[5] Many therapies are available with proven efficacy for reducing fracture risk in patients with osteoporosis. Among them, the oral bisphosphonates, including alendronate, risedronate, and ibandronate, are the most commonly used agents.

Oral bisphosphonates can cause irritation of the gastrointestinal (GI) tract[6]; however, the clinical relevance of endoscopic findings is uncertain.[7] Clinical trials have found that upper GI adverse events are no more frequent in bisphosphonate users than in recipients of placebo,[8–10] and several observational studies have found that GI events are as common before bisphosphonate use as after.[11–13] Studies of the frequency of GI events among patients who used oral bisphosphonates in real-world clinical practice have found that the experience of a GI event increases the likelihood of discontinuation,[14,15] and discontinuation precludes the reduction of fracture risk.

However, the understanding of the occurrence of GI events and characterization of GI events among patients who used oral bisphosphonates, particularly in the US-managed care population, is limited. It is important for treating physicians to know how many bisphosphonate users, and which ones, will experience GI events so that they can be ready with educational support and regimen adjustments to help these patients maintain their reduction in osteoporosis fracture risk. The objective of this study was therefore to determine the proportion and characteristics of US bisphosphonate users who experience GI events.

METHODS

Data Source

The retrospective cohort study was conducted with the i3 InVision Data Mart (i3, Ann Arbor, Michigan; now the Clinformatics Data Mart; Optum, Eden Prairie, Minnesota). This large, nationwide US claims database contains de-identified patient information, including demographic characteristics and medical and pharmacy claims data. Medical claims include *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis and procedure codes. The outpatient pharmacy claims data contain National Drug Codes for dispensed medications. More than 3 million patients with a diagnosis of osteoporosis, osteoporosis-related fracture, and/or a prescription for a medication used to treat or prevent osteoporosis were included in the database during the study period from January 2000 through December 2011.

Study Design

The index date, which could occur any time between January 1, 2001, and December 31, 2010, was defined as the date of the first oral bisphosphonate prescription. The pre-index period was the 12 months before the index date, and the post-index period was the 12 months after the index date. The analyses used de-identified patient data; thus, informed consent was not required.

Study Sample

Eligible patients were women aged $\geq$55 years with a diagnosis of osteoporosis (ICD-9 code 733.0), 1 new pharmacy claim for an oral bisphosphonate (alendronate, risedronate, or ibandronate) on the index date, and continuous enrollment in the health plan during the pre- and post-index periods. Patients were excluded if they had a pharmacy claim for any osteoporosis therapy at any time during the pre-index claims history, a medical claim for Paget disease (ICD-9 code 731.0x) at any time during the claims history, or a diagnosis of malignant neoplasm (ICD-9 codes 140.xx–171.xx, 174.xx–208.xx, or 230.xx–239.xx) during the pre- or post-index periods.

Study Variables

Patient age was assessed on the index date. Characteristics assessed within 1 year before the index date were the Deyo-Charlson comorbidity index score[16] and the use of gastroprotective agents, glucocorticoids, estrogen, and NSAIDs. Disease diagnoses and comorbidities were identified on the basis of ICD-9 codes, and medications were identified on the basis of National Drug Code numbers. Similar to previous publications,[12,13] GI events were identified on the basis of ICD-9 diagnosis codes for esophagitis; gastroesophageal reflux disease; ulcer, stricture, perforation, or hemorrhage of the esophagus; gastric, duodenal, or peptic ulcers; acute gastritis; duodenitis; GI hemorrhage; nausea/vomiting; or dysphagia. The following codes were defined as severe GI events: 530.21 (ulcer of the esophagus with bleeding), 530.4 (perforation of esophagus), 530.82 (esophageal hemorrhage), 531.x