Proportion and Characteristics of Patients in Sweden Remaining at High Risk of Fracture Despite Prior Treatment

Dan Mellström, MD[1]; Xiaoqin Yang, PhD[2]; Zhiyi Li, MA, MBA[3]; Chun-Po Steve Fan, PhD[4]; Ewa Waern, Research Fellow, MD[1]; Ankita Modi, PhD[2]; Shiva Sajjan, PhD[2]; and Stina Salomonsson, PhD[5]

[1]*Centre for Bone and Arthritis Research, University of Gothenburg, Gothenburg, Sweden;* [2]*Merck & Co., Inc., Kenilworth, New Jersey;* [3]*AsclepiusAnalytics LLC, New York, New York;* [4]*AsclepiusJT LLC, New York, New York; and* [5]*Merck Sharp & Dohme (Sweden), Stockholm, Sweden*

ABSTRACT

Purpose: Fragility fractures are a clinical consequence of osteoporosis (OP). Evidence suggests however, current OP treatments may be inadequate in reducing fracture risk. The purpose of this study was to estimate the proportion and characteristics of Swedish patients who remain at high risk of fracture after 2 years of treatment, as evidenced by osteoporotic bone mineral density (BMD), a decrease in BMD, or the occurrence of new fractures.

Methods: This was a retrospective, descriptive analysis of a subset of participants obtained from a Swedish osteoporosis patient registry from 1991 to 2009. Patients were required to be osteoporotic, to be treatment naive at baseline, to have returned for at least 1 follow-up visit, and to have reported osteoporosis treatment use for ≥2 years after the baseline visit with a BMD T score. Two overlapping cohorts remaining at high risk of fracture were defined using the BMD T score measured after 2 years of treatment from baseline. The osteoporosis cohort comprised patients who remained osteoporotic, whereas the BMD decrease cohort included patients whose total hip or lumbar spine T score decreased by ≥3%.

Findings: A total of 3292 osteoporotic patients were identified in the registry, of whom 392 met the study inclusion criteria. The mean (SD) patient age was 68.3 (8.5) years, with most patients being female (92.3%). Among all patients, 297 (75.8%) remained osteoporotic after at least 2 years of treatment, 90 (23.0%) experienced a BMD decrease of ≥3%, and 23 (5.9%) reported an incident fracture between the baseline and first follow-up visit. More than three-quarters (76.8%) of all patients reported taking bisphosphonates, whereas only 72.4% and 47.8% reported this in the osteoporosis and BMD decrease cohorts, respectively. Raloxifene was the only nonbisphosphonate used, with 24.2% of all patients reportedly taking it.

Implications: This study highlighted that despite 2 years of osteoporosis treatment, a high percentage of patients remain at high risk of fracture. There is a need for improved treatment strategies that reduce fracture risk and improve patient outcomes in the real-world setting. (*Clin Ther*. 2016;▮:▮▮▮–▮▮▮) © 2016 The Authors. Published by Elsevier HS Journals, Inc.

Key words: BMD, fracture, fracture risk, osteoporosis, treatment, treatment response.

INTRODUCTION

Osteoporosis is a skeletal disorder characterized by compromised bone strength and disruption of bone architecture that results in increased risks of fragility fractures, representing the predominant clinical consequence of osteoporosis. Fragility fractures contribute to the significant societal burden through the loss in quality of life attributable to associated pain, disability, substantial incremental health care costs, and higher mortality.[1]

The prevalence of osteoporosis is common in Sweden, with approximately 1 in 3 women aged 70

Accepted for publication May 10, 2016.
http://dx.doi.org/10.1016/j.clinthera.2016.05.005
0149-2918/$ - see front matter

to 79 years diagnosed as having osteoporsis.[2] In 2010, there were an estimated 107,000 incident fractures among Swedish adults 50 years and older, with most occurring among women (66%). By 2025, the annual fracture incidence is expected to increase by 26% to 135,000, primarily as a function of an aging population.[3] The health care costs associated with osteoporosis in Sweden are substantial. In 2005, the total annual fracture-related costs were estimated at 3.2% of total Swedish health care costs.[4] The economic burden is expected to continue to increase in Sweden from an estimated €1.5 billion in 2010 to €1.8 billion by 2025, an increase of 23%.[3]

The World Health Organization operationally defines osteoporosis as a bone mineral density (BMD) that is ≥2.5 SDs below the mean value for a healthy young adult (T score <−2.5 SDs).[1] Several pharmacologic therapies are available for patients with osteoporosis or at high risk of fracture.[5] For patients with osteoporosis, the aim of treatment is to slow the decrease in BMD and decrease fracture risk. In Sweden, osteoporosis treatments include bisphosphonates, estrogen agents, selective estrogen receptor modulators, parathyroid hormone, and denosumab.[2,6] Current Swedish guidelines for osteoporosis treatment are based on an algorithm that incorporates BMD T score, fracture risk,[7] and prior fracture.[6] Recommended treatments include alendronate as first-line therapy, zoledronic acid as second-line therapy, and risedronate and denosumab as alternative therapies. Raloxifene, strontium ranelate, teriparatide, and ibandronate are lower-priority treatment options.[6]

There is evidence to suggest that current osteoporosis treatment may be inadequate in reducing fracture risk, even under the well-controlled conditions of clinical trials.[8,9] There is no universally accepted definition of treatment failure; however, BMD decrease, incident fractures, and changes in markers of bone turnover are commonly used in clinical practice to measure fracture risk.[10] Diez-Perez and Gonzalez-Macias[8] reported that in 5 clinical trials[11–15] 8.0% to 12.4% of patients experienced fractures despite being treatment adherent (correctly taking at least 80% of doses). Observational evidence from Europe, Canada, and the United States found that 10% to 50% of patients experienced loss in BMD, persistently low BMD T scores, and/or fracture while undergoing active osteoporosis therapy.[9,16–21] For osteoporotic patients at high risk of fracture (ie, baseline BMD T score <−2.5), 25.8% experienced BMD decrease or multiple fractures.[9]

Swedish men and women have the second highest age-standardized risk of hip fracture in the world.[22] However, despite this high fracture rate, studies examining Swedish patients undergoing active osteoporosis therapy who are at high risk of fracture have not been published. Several studies conducted on patients in European countries have examined patients at high risk of fracture,[9,19,20,23,24] with most studies focusing exclusively on patients taking bisphosphonates,[9,17–21] neglecting the alternative nonbisphosphonate therapies available in Sweden.[6] To provide insight into the high fracture rate in Sweden, a retrospective study was conducted on a cohort of osteoporotic patients identified from a Swedish registry. The objective was to identify the proportion and characteristics of Swedish patients who remain at high risk of fracture after 2 years of active osteoporosis treatment, as evidenced by osteoporotic BMD, a decrease in BMD, or the occurrence of new fractures.

PATIENTS AND METHODS

Study Design

This study was a retrospective, descriptive analysis of data from a Swedish osteoporosis patient registry from 1991 to 2009. Studies that use data collected from patient registries may provide substantial information that contributes to the understanding of the incidence, treatment patterns, outcomes, and other descriptive characteristics of disease.[25] The registry was established at the osteoporosis clinic at Sahlgrenska University hospital in Gothenburg, a region in the west of Sweden that encompasses approximately 2 million people. Patients were referred to the osteoporosis clinic by general practitioners, gynecologists, and other providers of dual energy X-ray absorptiometry scans to assess BMD. This first clinic visit was classified as the baseline visit. On the basis of clinical recommendation, patients were referred back to the clinic for follow-up every 2 years. The first follow-up visit was the visit at least 2 years after the baseline clinic. Recommendations for follow-up visits were advised for patients diagnosed as having osteopenia (T score