Risedronate versus alendronate in older patients with osteoporosis at high risk of fracture: an Italian cost-effectiveness analysis

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ABSTRACT. Background and aims: This evaluation of the cost-effectiveness of risedronate vs generic alendronate is based on effectiveness data from a large real practice study. Applying a published cost-effectiveness model, we found that risedronate is cost-effective vs generic alendronate in an Italian population aged ≥65 years, and becomes dominant, saving costs and avoiding fractures, in patients aged ≥75 years. The aim of this work was to assess the cost-effectiveness and health utility of risedronate vs generic alendronate in clinical practice in Italy, using effectiveness data from the REAL study. Methods: A pre-existing model of osteoporosis was used to predict numbers of fractures, quality-adjusted life-years (QALYs), and costs associated with risedronate or alendronate treatment in post-menopausal (PMO) women aged ≥65 years with a previous vertebral fracture, within the Italian National Health System (NHS). Duration of treatment with risedronate or alendronate was assumed to occur for one year and patients were followed for an additional five years to capture long-term costs and outcomes, with a discount rate of 3% for costs and outcomes. Comprehensive sensitivity analyses were run. Results: The lower fracture rate among risedronate patients with respect to alendronate patients resulted in savings of €19,083, a reduction of 8.91 hip fractures and an associated benefit of 7.46 QALYs, in an Italian cohort of 1,000 patients. Sensitivity analyses confirmed the robustness of these results. Conclusions: This economic analysis showed that risedronate is a cost-effective treatment in a population of Italian women aged 65 years and older at high risk of PMO-related fractures. Risedronate becomes dominant over generic alendronate in patients of 75 years or older and its cost-effectiveness even appears improved in patients with BMD score ≤3 or ≤3.5, with/without maternal history of fractures. Risedronate should be considered as a cost-effective option vs generic alendronate, in the Italian NHS' perspective. (Aging Clin Exp Res 2010; 22: 179-188)

INTRODUCTION

Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and increased susceptibility to fractures, especially of the hip, spine and wrist. Osteoporosis occurs primarily as a result of normal aging, but is also attributed to impaired development of peak bone mass (e.g., due to delayed puberty or under-nourishment) or excessive bone loss during adulthood (1).

In 2006, almost four million Italian women were suffering from osteoporosis, 45% of them in the 70-79 age range. It is estimated that, by 2050, 4.7 million Italian women will develop osteoporosis (2).

In Italy, the number of hip fractures in excess of 80,000/year, 55% of which occur in women (45% in men) and 33% in women over 65 years of age (2, 3). Fractures severely affect the quality of life: 20% of all subjects who suffer hip fractures die within one year of the event, 30% are affected by permanent disability, 40% are not able to walk independently, and 50% are not able to carry on activities of daily living (2, 4). In general, survival is dramatically reduced by hip fractures: mortality is reported as 50% after 2 years and 25% after 4 years. In addition to the influence on quality of life, osteoporosis also carries a considerable medical and financial burden, the largest component of direct costs being related to fracture treatment. In 2005, these costs were estimated to be 17 billion dollars in the US (5).
the European Union (EU), osteoporosis annually costs more than € 6.3 billion in hospital care alone (6). An Italian study compared 1999-2002 direct costs (excluding rehabilitation) of osteoporosis and myocardial infarction, and showed that hospital admission costs for hip fractures in subjects over 45 years are higher, i.e., in the range of 417-510 million Euros for hip fractures vs € 400-410 million for myocardial infarction, respectively (7). Total costs (i.e., admission, rehabilitation, disability pensions and indirect costs) were found to be slightly over € 1 billion for fractures, comparable to the costs of acute myocardial infarction, in subjects over 65 years of age (7). Another Italian study reported social costs of osteoporosis in the range of € 1.1 billion, 806 million of which were due to direct costs (full admission and post-surgical rehabilitation), € 108 million to indirect costs (disability pensions and caregiver subsidies for 18,000 disabled/years) and the remaining € 183 million to other indirect costs (3). Public expenditure for subjects at risk of osteoporosis is predicted to increase from the current € 1,730/patient to € 2,555/patient in 2020, and up to € 4,926/patient in 2050 (2). The risk of recurrences is also high and costly: 25% of hip fracture patients may incur a second event, and Italian estimates show that, of 60,800 subjects living after first hip fracture, 15,200 may be at risk of further events, at an estimated additional cost of € 206 million (2).

All the bisphosphonates have been shown to reduce the incidence of fractures, significantly and with good safety profiles: their efficacy as regards fracture prevention has been established in large-scale trials lasting 3-4 years (8-13). Risedronate and alendronate are the only pharmacological therapies for osteoporosis with clinical trial data extending beyond 5 years, to address the issue of long-term efficacy. The VERT Multinational study demonstrated the maintained effects of long-term efficacy of risedronate vs placebo over 3 years of treatment on a population of 1,226 post-menopausal women (14). Risedronate has also demonstrated “unexpectedly high” levels of persistence as the IMPACT (Improving the Measurement of Persistence on Actonel treatment) study has shown; in addition, patients were more likely to remain on treatment whenever their response to therapy improved, as assessed by their physicians by measurement of Bone Turnover Markers (BTMs) (15).

Risedronate has been shown to reduce the risk of hip fractures among elderly osteoporotic women within a clinical trial designed to evaluate as primary end-point the incidence of radiographically confirmed hip fractures (16). This efficacy has also been confirmed in real life by an observational study (REAL) among women aged 65 and over, treated with once-a-week doses of either risedronate or alendronate (17).

In the field of osteoporosis, economic analysis can be used to answer various questions, such as: which treatment should be used, taking into account both costs and effects of the various treatments? In order to answer this question, the costs of intervention must be weighed against the benefits of treatment. For PMO, possible costs and cost offsets are those associated with preventive drug therapy, treatment of fractures (i.e., hospitalization, rehabilitation, outpatient visits), and the side-effects of drug therapies. Benefits include reduced morbidity (i.e., reduction in number of fractures), increased quality of life, and reduced mortality.

The Clinical and Economic Impact of Osteoporosis (CLIO) model, whose general structure was described in 2001 (18), has been extensively used to evaluate the cost-effectiveness of risedronate vs different comparators in a number of economic analyses in many countries (19-26). Based on a Markov state transition model, the purpose of which was to assess the cost-effectiveness of competing PMO interventions among population subgroups (e.g., age-ranges, risk levels) within a diverse group of countries, the model simulates the natural history of osteoporosis in women aged from 50 to 100 years, and estimates the effects of treatment on fracture occurrence, fracture-related and all-cause mortality, quality-adjusted life-years (QALYs) and costs of osteoporosis-related health events (i.e., fractures) (18).

Using this model, we performed an economic analysis with the aim of assessing the comparative cost-effectiveness (cost-effectiveness analysis: CEA) of risedronate vs generic alendronate on Italian women aged 65-99 years, at high risk of PMO-related fractures, in the perspective of the Italian National Healthcare System (NHS).

**METHODS**

The CLIO Model considers five long-term health states (Healthy, Healthy Post-Hip Fracture, Healthy Post-Vertebral Fracture, Healthy Post-2nd Hip Fracture, and Deceased) used to model long-term disease progression, and four short-term health states (Hip Fracture, Vertebral Fracture, Wrist Fracture, and Other Fracture) used to capture, for each given year, the probability of undergoing these events on costs and clinical outcomes (fractures and QALYs) (18). The model facilitates economic evaluation of drug treatment on populations at increased risk of fracture, due to the presence of one or more risk factors. The population profile is defined according to population size, starting age, bone mineral density (BMD) score, and risk factor profile (i.e., maternal history of hip fracture, previous vertebral fracture). In particular, our analysis focused on population sizes of 1,000 patients entering the model at the age of 65-99 years, evaluated by five-year age cohorts, with previous history of vertebral fracture and Bone Mineral Density (BMD) ≤ 2.5, i.e., a large subset of all PMO women who qualify for reimbursement in Italy under Note 791.