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Cost-effectiveness of strontium ranelate versus risedronate in the treatment of postmenopausal osteoporotic women aged over 75 years

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ABSTRACT

Objective: To estimate the cost-effectiveness of strontium ranelate in the treatment of postmenopausal osteoporotic women aged over 75 years.
Materials and methods: A validated Markov microsimulation model with a Belgian payer's perspective estimated the cost per quality-adjusted life-year (QALY) of a 3-year strontium ranelate treatment compared with no treatment and with the bisphosphonate risedronate. Data on the effect of both treatments on fracture risk were taken from the Cochrane Database of Systematic Reviews. Analyses were performed for postmenopausal women aged 75 and 80 years, either with a diagnosis of osteoporosis (i.e. bone mineral density *T*-score ≤ -2.5 SD) or with prevalent vertebral fractures (PVF). Parameter uncertainty was evaluated using both one-way and probabilistic sensitivity analyses.
Results: Strontium ranelate was dominant (i.e. more effective and less costly) versus risedronate for women with osteoporosis aged over 75 years and for women with PVF aged 80 years. The cost per QALY gained of strontium ranelate compared with risedronate at 75 years of age was €11,435 for women with PVF. When compared with no treatment, the costs per QALY gained of strontium ranelate were €15,588 and €7,708 at 75 and 80 years of age for women with osteoporosis; the equivalent values were €16,518 and €6,015 for women with PVF. Probabilistic sensitivity analyses showed that strontium ranelate was generally more cost-effective than risedronate, in the range of 60% in all cases.
Conclusion: The results of this study suggest that strontium ranelate is a cost-effective strategy, in a Belgian setting, for the treatment of postmenopausal osteoporotic women aged over 75 years.

Introduction

Osteoporosis is a common disease characterized by low bone mass and deterioration of bone tissues, resulting in increased bone fragility and fracture risk. Osteoporotic fractures are a significant cause of morbidity and mortality, particularly in the developed countries and impose a huge financial burden on health-care systems [1].

Many agents have been developed for the management of postmenopausal osteoporosis. Oral bisphosphonates are well established for osteoporosis management, and have been shown to reduce the risk of vertebral and non-vertebral fractures [2]. However, for daily and weekly formulations, adherence remains poor and limits their benefits in routine clinical practice [3]. Strontium ranelate has recently been introduced for the treatment of osteoporosis. Strontium ranelate was found to simultaneously decrease bone resorption and stimulate bone formation in vitro [4], and to significantly reduce the risk of vertebral and non-vertebral fractures in a wide range of patient profiles and over a long-period of time [5–8]. In addition to the therapeutic value of a drug, it is becoming increasingly important to evaluate the cost-effectiveness compared with the most relevant alternative treatment. Cost-effectiveness analysis is commonly used to help allocate economic resources in a more efficient manner [9], and the results often guide healthcare decisions and assist physicians in comparing alternative strategies.

Previous studies have shown strontium ranelate to be cost-effective in the treatment of postmenopausal osteoporosis [10–12]. In a Swedish-based study, strontium ranelate was cost-effective compared with no treatment for postmenopausal women with low bone mineral density and who are similar to patients included in the clinical trials or even cost-saving in patients over 80 years old [10]. Recently, long-term treatment with strontium ranelate over 5 years was shown, in a Belgian setting, to be cost-effective compared with no treatment in the target populations for routine use of the product [11], and strontium ranelate was cost-effective in the treatment of established osteoporosis in UK women over the age of 65 years [12]. These studies were however restricted to the comparison of strontium ranelate versus no treatment. For decision-makers, it would be useful to compare strontium ranelate with other treatments, such as oral bisphosphonates. The cost-effectiveness of a treatment should ideally

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be compared with the most relevant alternative [13]. No one comparator has however been universally used in economic evaluations of osteoporosis medications [14]. The main reason is that no direct comparison between treatments is available, making it difficult to assess the relative efficacy. Cost-effectiveness between treatments can only be estimated by making indirect comparisons.

The objective of this study was to assess the cost-effectiveness of strontium ranelate compared with no treatment and with the bisphosphonate risedronate in the treatment of postmenopausal Belgian osteoporotic women over 75 years old. Risedronate is currently registered in Europe for the treatment of osteoporosis and has been shown to significantly reduce the risk of fractures in postmenopausal women with osteoporosis [15–17]. It is currently the only bisphosphonate investigated in a population of elderly women, with hip fracture reduction used as the primary endpoint [15]. Subsequently, risedronate is the comparator of choice for the current study, based on its age-perspective as well as based on the results obtained on hip fracture reduction, in a subset of the TROPOS trial population, including women with osteoporosis and aged over 74 years [7]. The cost-effectiveness of risedronate compared with no treatment in women with osteoporosis has been demonstrated in several countries [18–20], but the cost-effectiveness of risedronate has never been tested against any other active medication, in women aged 75 years and older.

Materials and methods

Simulation model

Cost-effectiveness analysis was performed using a Markov microsimulation model, which has been validated elsewhere [21]. The model has also been used to estimate the effects of changes in baseline population risk and changes in life expectancy on absolute lifetime fracture risks [22], as well as to assess the cost-effectiveness of osteoporosis screening [23,24].

This study was performed from a payer's perspective, including direct healthcare costs paid by the national health insurance and the individual patient's out-of-pocket contribution, in accordance with Belgian methodological guidelines for pharmacoeconomic evaluations [25].

The cycle length of the model was set to 1 year and a patient lifetime horizon was used, as recommended [26,27]. Beginning in the no fracture state, each patient had, every year, a certain probability of the following events: hip, clinical vertebral, wrist, or other fracture; no fracture; or death. The incidence of hip fracture was derived from a Belgian study, and the incidence of other fractures was imputed using fracture rates from other countries, assuming that the ratio between hip and other fractures would be similar between countries [22]. Each state had an associated cost and effectiveness, depending on patient characteristics. Transition costs included direct fracture costs in the year following the fracture and long-term costs beyond the first year for women institutionalized after a hip fracture. The direct cost of hip fracture was derived from Belgian studies [28,29] and the costs of clinical vertebral and other fracture were quantified relative to hip fracture on the basis of their costs [30,31]. Effectiveness was expressed in quality-adjusted life years (QALYs). The QALY estimator is an attractive outcome measurement in the field of osteoporosis because it offers the advantage of capturing the benefits from reductions in both morbidity and mortality [32]. Fracture disutility was modelled as a lower value for QALY and was derived from a systematic review of the literature [33]. Excess mortality was also assumed after hip and clinical vertebral fractures. Discount rates of 3% and 1.5% were assumed for cost (expressed in €2006) and effectiveness, respectively [25]. A detailed description and explanation of the model and data has been published elsewhere [21].

Target populations

Cost-effectiveness analyses were performed in two populations for whom osteoporosis medications are currently reimbursed in Belgium, i.e. women with a diagnosis of osteoporosis (BMD *T*-score ≤ -2.5 SD) and women with prevalent vertebral fractures (PVF). In order to accurately reflect the fracture risk in these populations, the risk of first fracture in the general population [22] was adjusted by a relative risk (RR).

The RR for all osteoporotic women was estimated using a previously validated method [34], which estimates the risk of individuals below the threshold value compared with the fracture risk in the general population of that age. This is therefore appropriate for considering a group of individuals such as all women with osteoporosis [34]. BMD values were derived from the recommended NHANES III [35] database at the femoral neck, and one SD decrease in BMD was associated with an RR of 1.8, 1.4 and 1.6 for clinical vertebral, forearm, and other osteoporotic fracture, respectively [36]. For hip fracture, the RR ranged from 3.68 at 50 years to 1.93 at 85 years [37].

The RRs for patients with PVF were 2.3, 4.4, 1.4, and 1.8 for hip, clinical vertebral, wrist, and other fracture, respectively [38]. These RRs were reduced by 10% per decade above the age of 70 years [39]. For women with PVF, no additional increase in fracture risk was assumed for further fractures during the simulation process.

Interventions

Data on the effect of both treatments on fracture risk were taken from the Cochrane Database of Systematic Reviews [40,41]. (Table 1) Strontium ranelate was assumed to reduce the risk of clinical vertebral fracture by 38% (RR 0.62, 95% confidence interval (CI) 0.47–0.83) and the risk of wrist and other fracture by 19% (RR 0.81, 95% CI 0.66–0.98) versus placebo, using the fracture risk reduction estimated for major nonvertebral fracture [40]. The effect of strontium ranelate on hip fracture was derived from a subgroup of women at high risk of hip fracture (i.e. women aged 74 years and older with a femoral BMD *T*-score ≤ -2.4 SD according to NHANES III). The RR for hip fracture was therefore 0.64 (95% CI 0.41–0.99). For risedronate, the RRs versus placebo were 0.60 (95% CI 0.50–0.76) for vertebral fracture, 0.74 (95% CI 0.59–0.94) for hip fracture, 0.67 (95% CI 0.42–1.07) for wrist fracture, and 0.80 (95% CI 0.72–0.90) for other fracture [41].

Patients were treated for 3 years as in the clinical trials and the treatment effect was instantaneous. After stopping therapy, the risk reduction was assumed to decline in a linear manner over a 3-year period, denoted the offset time, in line with clinical studies [42,43].

The annual costs of drug therapy were estimated at €512.48 for strontium ranelate (Protelos®, €117.94 for a pack of 84 sachets [44]) and at €422.31 for risedronate (Actonel®, €97.19 for a pack of 84 tablets [45]). The costs of one yearly physician visit (estimated at €20) and of a BMD measurement at years 1 and 3 (estimated at €47) were also assigned. We also assumed that patients were fully adherent and had no adverse events in the base-case analysis.

Table 1
Treatment effect expressed as relative risk at the sites shown and annual cost of therapy.

Parameters	Strontium ranelate	Risedronate
Relative risk of fracture during therapy	[40]	[41]
Hip fracture	0.64 (95% CI 0.41–0.997)	0.74 (95% CI 0.59–0.94)
Vertebral fracture	0.62 (95% CI 0.47–0.83)	0.60 (95% CI 0.50–0.76)
Wrist fracture	0.81 (95% CI 0.66–0.98)	0.67 (95% CI 0.41–1.07)
Other fracture	0.81 (95% CI 0.66–0.98)	0.80 (95% CI 0.72–0.90)
Annual therapy cost	€ 512.48 [44]	€ 422.31 [45]

CI = confidence interval.