A Comparison of the Cost-Effectiveness of Bisphosphonates Using Persistence Data from a UK Prospective Randomized Control Trial

S.R. Earnshaw,[1] S.M. Beard,[2] N.O. Lynch,[3] A. Cooper,[4] W. Cowell,[5] and H. Middelhoven[6]

[1]RTI Health Solutions, Research Triangle Park, NC, USA; [2]RTI Health Solutions, Manchester, UK; [3]GlaxoSmithKline, Middlesex, UK; [4]Crawley, UK (on behalf of PERSIST study investigators); [5]Roche Products Ltd, Welwyn, UK; [6]F. Hoffmann-La Roche AG, Basel, Switzerland

ABSTRACT

The objective was to estimate the cost-effectiveness of monthly ibandronate compared to weekly alendronate for women with postmenopausal osteoporosis in the United Kingdom (UK), based on persistence data from PERSIST, a UK prospective randomized control trial. A Markov model was developed to evaluate the lifetime cost-effectiveness of monthly oral ibandronate and weekly alendronate. Vertebral, hip, and wrist fracture efficacy were assigned a bisphosphonate class effect as estimated by the literature. Persistence rates from PERSIST were input into the economic model. Monthly ibandronate had 57% persistence at 6 months vs 39% for weekly alendronate. These persistence rates were then extrapolated, based on UK GPRD data, to represent a continued decline in persistence up to five years, the assumed maximum time on therapy. The analysis population was postmenopausal women aged ≥50 years with prevalent radiologic vertebral deformity and a hip bone mineral density (BMD) T-score ≤−2.5. Yearly drug costs were referenced to acquisition cost for each bisphosphonate. Direct health resource costs for fracture states were estimated from published literature and discounted at a 3.5% yearly rate. All costs were reported in 2004 £UK.

More fractures were avoided (vs no treatment) with monthly ibandronate (10.3 per 1,000 women) than with weekly bisphosphonates (4.8 per 1,000 women), resulting in 12.5 additional quality-adjusted life years (QALYs) per 1,000 patients using ibandronate vs 6 additional QALYs per 1,000 patients using weekly bisphosphonates. Under conditions of higher persistence with monthly ibandronate, drug costs per patient are higher with ibandronate than with alendronate (£310 vs £249 per annum, respectively). However, these costs are offset by lower medical costs—£6,286 for ibandronate vs £6,359 for alendronate. The incremental cost per QALY gained (vs no treatment) was significantly lower for monthly ibandronate (£13,691) compared to alendronate (£30,450). Since the overall costs are lower with ibandronate, the incremental cost per QALY gained is more effective and less costly than weekly alendronate. Compared to alendronate, ibandronate is a cost-effective intervention for the treatment of postmenopausal osteoporosis. Compared to alendronate, incremental persistence with monthly ibandronate, as seen in the PERSIST study, improves the potential benefit for patients while reducing the overall costs of treatment.

METHODS

A Markov model (Figure 1) was used to simulate a cohort of postmenopausal women aged ≥50 years with a prevalent radiologic vertebral deformity and a hip bone mineral density (BMD) T-score of ≤−2.5 (Table 1).
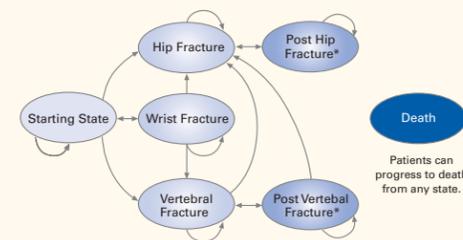
Parameters and Assumptions

- Patients transition between the health states based on published data (Stevenson et al., 2005; Klotzbeucher et al., 2000; Office of National Statistics, 2004; Johnell et al., 2004).

- Postmenopausal population is assumed to be represented by those aged ≥50 years (Table 1).

- Perspective was payer.

- Treatment options considered: monthly ibandronate, weekly alendronate, no treatment.

- Bisphosphonate class effect applied for fracture reduction: vertebrae (43%), hip (33%), and wrist (17%) (Kanis et al., 2002).

- Full efficacy achieved after 12 months of treatment.

- Maximum time on treatment was 5 years.

- Post treatment efficacy declined in proportion to time on treatment.

- Direct healthcare costs inflated to 2004 (Kanis et al., 2002; Dolan et al., 1998).

- Utilities for fracture states (Brazier et al., 2002; Tosteson et al., 2001).

- Discounting of costs and benefits at 3.5% per annum.

- Annual drug costs: £252 ibandronate and £296 alendronate (British National Formulary).

Persistence Data

- In PERSIST study, ibandronate treatment included a Patient Support Programme (PSP).

- Persistence at 6-months: 57% (ibandronate+PSP) and 39% (alendronate) based on the PERSIST trial in postmenopausal osteoporotic women (Cooper et al., 2006).

Figure 1. Model Structure

Starting State, Hip Fracture, Post Hip Fracture*, Wrist Fracture, Vertebral Fracture, Post Vertebral Fracture*, Death

Patients can progress to death from any state.

* For simplification, we assume that once patients experience a hip fracture or vertebral fracture they can experience no further wrist fractures. Patients in the post-hip-fracture state can experience further vertebral fractures through a state prevalence estimate.

Table 1. Parameters Used in the Model

Parameter	Source
Age distribution of women in the UK	Office of National Statistics, 2004
Mean bone mineral density T-scores among osteoporotic women by age group	Stevenson et al., 2005; Holt et al., 2002
Prevalence of prior fractures among age groups	O'Neill et al., 1996
Fracture history by age and fracture type among females with prior fracture	Kanis et al., 2002
Prevalence of osteoporosis (T-score ≤−2.5)	Kanis et al., 2000

- Persistence rates extrapolated over 5 years using long term drug utilization patterns for weekly and daily bisphosphonate use, as observed in the UK General Practice Research Database (GPRD) (Brankin et al., 2006).

- Extrapolation based on a Weibull distribution.

- Extrapolation based on an approximated 40% relative improvement in persistence with weekly bisphosphonates over treatment with a daily formulation.

- Sensitivity analyses were performed around the expected improvement in persistence for monthly ibandronate.

RESULTS

Modeled results in terms of fractures avoided, per-patient costs, and cost-effectiveness are presented in Table 2 and Figure 2.
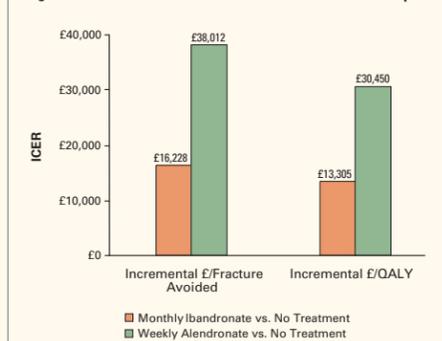
Table 2. Estimated Fractures Avoided per 1,000 Patients and Average Costs per Patient

Outcome	Monthly Ibandronate	Weekly Alendronate
Number of fractures avoided per 1,000 patients		
Hip	3.09	0.99
Vertebral	5.71	0.86
Wrist	1.49	0.86
Total	10.30	4.82
Average costs per patient treated (UK £)		
Drug	£ 310	£ 249
Fracture care	£ 6,286	£ 6,359
Total	£ 6,596	£ 6,608

Note: With no treatment, 108 hip fractures, 69 vertebral fractures, and 48 wrist fractures are incurred per 1,000 patients.

- A 40% relative improvement in persistence more than doubles the number of fractures avoided.

- Improved persistence resulted in 12.5 additional QALYs per 1,000 patients on monthly ibandronate versus 6.0 additional QALYs per 1,000 patients on weekly alendronate.

- Increased persistence does result in increased drug costs, but the reduction in fractures with monthly ibandronate results in a reduction in fracture care costs compared to weekly bisphosphonates.

- Lower total costs result due to increased persistence.

Figure 2. Incremental Cost-Effectiveness Ratios for Selected Endpoints

Incremental £/Fracture Avoided: Monthly Ibandronate vs. No Treatment £16,228; Weekly Alendronate vs. No Treatment £38,012. Incremental £/QALY: Monthly Ibandronate vs. No Treatment £13,305; Weekly Alendronate vs. No Treatment £30,450.

■ Monthly Ibandronate vs. No Treatment ■ Weekly Alendronate vs. No Treatment

- With a 40% improvement in persistence, the incremental cost-effectiveness ratios (ICERs) are well within acceptable thresholds of cost-effectiveness.

- Monthly ibandronate is more effective and less costly than weekly alendronate in the presence of persistence.

Sensitivity Analysis

A sensitivity analysis was performed for monthly ibandronate around the change persistence expected due to the monthly formulation of ibandronate (Figure 3).

Figure 3. Sensitivity Analysis of Estimated Fractures Avoided per 1,000 Patients for Changes in Persistence with Monthly Ibandronate
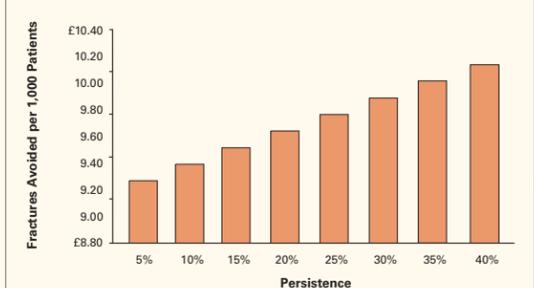
- Small improvements in persistence produce clinical benefits in terms of decreased number of fractures.

CONCLUSIONS

- Treating postmenopausal, osteoporotic women with monthly ibandronate is cost-effective.

- Even with small improvements in persistence, monthly ibandronate is more effective and less costly than weekly alendronate.

- Model results consider direct costs only. The addition of societal costs is likely to further improve the cost-effectiveness of all bisphosphonate treatments.

- Greater fracture reduction is seen when persistence is improved.

REFERENCES

Brankin E et al. *Current Medical Research and Opinion* 2006; 22 (7):1249–1256.

Brazier JE et al. *Osteoporos Int* 2002; 13:768–76.

British Medical Association and Royal Pharmaceutical Society of Great Britain. British National Formulary (BNF) 51. http://www.bnf.org; 2006.

Cooper A et al. *Int J Clin Pract* 2006;1–10.

Dolan P et al. *Osteoporos Int* 1998; 8(6):611–7.

Holt G et al. *Br J Radiol* 2002; 75(897):736–42.

Johnell O et al. *Osteoporos Int* 2004; 15:38–42.

Kanis JA et al. *Health Technol Assess* 2002; 6(29).

Kanis JA et al. *Osteoporos Int* 2000; 11:669–74.

Klotzbeucher CM et al. *J Bone Miner Res* 2000; 15:38–42.

O'Neill TW et al. *J Bone Miner Res* 1996; 11:1010–8.

Office of National Statistics. Key Population and Vital Statistics. Series VS No. 31, PP1 No. 27 (www.statistics.gov.uk); 2004.

Stevenson M et al. 2005. The National Institute for Clinical Effectiveness. http://www.nice.org.uk/pdf/Assessment_report_osteo.pdf.

Tosteson ANA et al. *Osteoporos Int* 2001; 12:1042–9.

CONTACT INFORMATION

Stephanie Earnshaw, PhD
U.S. Head of Health Economics

RTI Health Solutions, RTI International
3040 Cornwallis Road, PO Box 12194
Research Triangle Park, NC 27709-2194

Phone: 919-485-2730
Fax: 919-541-7222
E-mail: searnshaw@rti.org

Presented at: American Society for Bone and Mineral Research (ASBMR) 28th Annual Meeting

September 15–19, 2006, Philadelphia, PA, USA
http://www.asbmr.org/meeting/index.cfm