ORIGINAL PAPER

A comparison of the effect of alendronate and risedronate on bone mineral density in postmenopausal women with osteoporosis: 24-month results from FACTS-International

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SUMMARY

Objectives: To compare alendronate 70 mg once weekly (OW) with risedronate 35 mg OW with respect to change in bone mineral density (BMD), biochemical markers and upper gastrointestinal (UGI) tolerability over 24 months. **Methods:** This was a 12-month extension to the Fosamax® Actonel® Comparison Trial international study (FACTS). Postmenopausal women with osteoporosis randomly assigned to either alendronate 70 mg OW or risedronate 35 mg OW for the 12-month base study continued taking the same double-blind study medication. Efficacy measurements were BMD at the hip trochanter, lumbar spine, total hip, and femoral neck and levels of four bone turnover markers at 24 months. The primary hypothesis was that alendronate would produce a greater mean per cent increase from baseline in hip trochanter BMD at 24 months. **Results:** Trochanter BMD increased significantly from baseline to month 24 in both groups, with a significantly larger increase with alendronate: adjusted mean treatment difference of 1.50% (95% confidence interval: 0.74%, 2.26%; p < 0.001). Similar results were seen at all BMD sites. Significant geometric mean per cent decreases (p < 0.001) from baseline were seen for all four bone turnover markers in both groups, with significantly larger decreases (p < 0.001) with alendronate: adjusted mean treatment differences ranged from 8.9% to 25.3%. No significant differences were seen in incidence of UGI or other adverse events. **Conclusions:** Alendronate 70 mg OW yielded significantly greater BMD gains and larger decreases in bone turnover marker levels than risedronate 35 mg OW over 24 months, with no difference in UGI tolerability.

What's known
The bisphosphonates (alendronate, risedronate and, in some countries, ibandronate) are currently the preferred therapy for the treatment of osteoporosis. These agents effectively decrease bone resorption, increase bone mineral density (BMD), and reduce the risk of both vertebral and non-vertebral fractures. Alendronate has been shown to produce significantly greater increases in BMD and reductions in biochemical markers of bone turnover than risedronate in three head-to-head studies.

What's new
In two of the head-to-head trials of alendronate vs. risedronate, conducted in the USA (FACT) and in an international study (FACTS), postmenopausal women with osteoporosis were randomised to alendronate 70 mg taken once weekly or risedronate 35 mg once weekly. Both studies were conducted over a 12-month period, and both trials also conducted a 1-year extension to determine if the differences in BMD and turnover persisted over 2 years and if tolerability remained similar. This report provides the results from the 1-year extension of the international trial, encompassing 2 years of treatment.

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Introduction

Osteoporosis is a disorder usually characterised by increased bone turnover and an excess of bone resorption over formation, leading to decreases in bone density, reduced bone strength and increased fracture risk. The bisphosphonates (alendronate, risedronate and, in some countries, ibandronate) are currently the preferred therapy for the treatment of osteoporosis (1). These agents effectively decrease bone resorption, increase bone mineral density (BMD), and reduce the risk of both vertebral and non-vertebral fractures. The magnitude of change in bone turnover and BMD during antiresorptive ther-

apy has been correlated with the reduction in fracture risk (2–10). Among antiresorptive agents, only those that produce relatively large effects on BMD and bone turnover have convincingly demonstrated reductions in both vertebral and non-vertebral fracture risk.

Alendronate (FOSAMAX®, Merck & Co., Inc., Whitehouse Station, NJ) is a nitrogen-containing bisphosphonate that selectively inhibits osteoclast-mediated bone resorption. Large placebo-controlled clinical trials have shown BMD increases of approximately 9% at the spine and 6% at the hip with 10 mg alendronate daily for 3 years (11,12). Long-term follow-up of the phase III studies of alendro-

nate have demonstrated that spine BMD increases progressively for at least 10 years, and the initial BMD increases with alendronate treatment at other skeletal sites are maintained during long-term therapy (13,14). In addition, bone turnover markers are reduced into the normal premenopausal range within months after treatment and remain stable for at least 10 years, without evidence of progressive declines (14). Treatment with alendronate reduced the risk of vertebral fractures by 48% compared with placebo consistently across studies that included different populations; a 37–55% risk reduction was observed for non-vertebral (including hip) fractures across different populations with osteoporosis (15,16). These fracture risk reductions were observed within 6–18 months after initiating therapy (17–19).

Risedronate (ACTONEL®, Procter & Gamble Pharmaceuticals and Sanofi-Aventis, Paris, France) is a pyridinyl bisphosphonate that, like alendronate, binds to bone hydroxyapatite and inhibits osteoclast-mediated bone resorption. In postmenopausal women with osteoporosis and prior vertebral fracture, increases in BMD over 3 years with risedronate 5 mg daily were approximately 5% at the lumbar spine, 2% at the femoral neck and 3% at the hip trochanter (20). Reductions in biochemical markers of bone turnover during daily risedronate therapy were observed (20), albeit to a lesser extent than the reductions achieved with alendronate, but such differences may be partly related to different assay techniques or other factors. Vertebral and non-vertebral fracture risk reductions of approximately 36% and 19–27%, respectively, have been reported in meta-analyses of data from randomised trials of risedronate in women with osteoporosis (21,22). As with alendronate, fracture risk reductions were observed within the first year of risedronate treatment.

Direct head-to-head studies with clinically relevant end-points are the best method by which to compare the efficacy of different therapeutic agents (23). An ideal comparison of agents for osteoporosis would include fracture as an end-point. However, such a study is impractical because of the enormous cost and resources that would be required. For instance, more than 50,000 patients would be required to show a difference in fracture rates of at least 10%, assuming a 1-year fracture incidence of 5% (24). In the absence of head-to-head fracture data, comparative studies with validated surrogate end-points provide alternative evidence (25,26). Measurements of BMD and bone turnover markers are considered by some to be appropriate surrogates, because the magnitude of change in these measures during treatment with antiresorptive agents is associated with relative reductions in fracture risk (3,10).

Alendronate has been shown to produce significantly greater increases in BMD and reductions in biochemical markers of bone turnover than risedronate in three head-to-head studies. In the first trial, patients were randomised to alendronate 70 mg taken once weekly (OW) while fasting or risedronate 5 mg taken daily 2 h after a meal (as suggested by the manufacturer and approved in most countries) (27). Subsequently, weekly dosing with risedronate 35 mg became available and was used in the second and third trials, conducted in the USA (Fosamax Actonel Comparison Trial, FACT) (28) and in an international study (FACTS) (29). Both studies were conducted over a 12-month period, and both trials also conducted a 1-year extension to determine if the differences in BMD and turnover persisted over 2 years and if tolerability remained similar. This report provides the results from the 1-year extension of the international trial, encompassing 2 years of treatment.

Methods

Patient enrolment

Participants in FACTS-international were community-dwelling, ambulatory, postmenopausal (≥ 6 months from cessation of menses) women ≥ 40 years of age (≥ 25 years if rendered menopausal surgically) with a BMD ≥ 2.0 standard deviations (SD) below young normal mean bone density ($T \leq -2.0$) in at least one of four sites [total hip, hip trochanter, femoral neck or postero-anterior (PA) lumbar spine (L1–L4)]. The women were otherwise required to be in good general health, with hip and spinal anatomy suitable for dual-energy X-ray absorptiometry (DXA). In accordance with alendronate prescribing information, individuals with a history of abnormalities of the oesophagus that delay oesophageal emptying, such as stricture or achalasia, were excluded, as were those unable to remain upright for 30 min after dosing. The specific exclusion criteria have been published previously (29). Women with hypocalcaemia, hypovitaminosis D [serum 25(OH)D < 10 ng/ml], or metabolic bone diseases other than postmenopausal osteoporosis also were excluded. Women who completed the original 12-month study were eligible to enter the extension study.

Study design

The extension (Protocol 907–10) was a double-blind, active-controlled, multicenter study during which all eligible women maintained their original randomised, blinded treatment allocation from year 1 (oral alendronate 70 mg OW or oral risedronate 35 mg

OW) for an additional 12 months. Seventy-two of the original 75 international sites chose to participate in the extension study. Throughout the entire 12-month extension of the study, the investigator, patient, Central Laboratory and BMD Quality Assurance Center remained blinded to treatment group allocation; the sponsor did not remain blinded to treatment allocations, laboratory results or BMD results after the unblinding of the database for the analyses of the base study. The study was conducted in accordance with consideration for the protection of patients, as outlined in the Declaration of Helsinki, and was approved by the appropriate institutional review boards. All participants gave written, informed consent before entering the study extension.

Details of the design of the base study (Protocol 907) have been described (27). Women eligible to enter the extension study were to begin treatment within 7 days after their final year 1 study visit and to take their dose of study medication on the same day each week. In addition to study medication, all patients were instructed to consume 1000 mg of elemental calcium and 400 international units of vitamin D daily, either from their pre-existing diet or a supplement provided by the sponsor (Os-cal 500 + D®; SmithKline Beecham, Pittsburgh, PA) with their noon or evening meals. Women recorded medication use during the 24 months of treatment.

Assessment of outcomes

Bone mineral density was measured by DXA using Hologic or Lunar densitometers on the same machine during baseline and at all follow-up visits to the investigational site through month 24. Instrument quality control and all BMD analyses were performed by the BMD Quality Assurance Center blinded to treatment allocation. No significant machine drifts or shifts occurred during the 2-year study based on phantom BMD measurements on each dual-energy X-ray absorptiometer.

Two markers each of bone resorption and bone formation were used to evaluate changes in bone turnover. The bone resorption marker assays were urinary *N*-telopeptide of type I human collagen (NTX) corrected for creatinine (Ortho Vitros; Ortho Clinical Diagnostics, Amersham, UK) and serum C-telopeptide (CTX); (Roche Elecsys, measured on the Elecsys 2010 automated analyser, Manheim, Germany). The bone formation marker assays were serum bone-specific alkaline phosphatase (BSAP) (Access OSTASE Assay, Beckman-Coulter, Fullerton, CA) and serum N-terminal propeptide of type 1 procollagen (P1NP); (INTACT P1NP; Orion Diagnostic, P1NP RIA, Espoo, Finland). Samples for serum bio-chemical markers and a fasting second morning void for urinary NTX were obtained at 24 months. Stored samples were analysed in batches by time point at the end of the study.

Efficacy and safety evaluations

The primary efficacy end-point was the comparison of the mean percentage change from baseline in hip trochanter BMD at 24 months between the two treatment groups. Secondary BMD end-points included a comparison of the mean percentage change from baseline in total hip, femoral neck, and lumbar spine BMD at 24 months between the two treatment groups and the proportion of patients with predefined increases of hip trochanter and lumbar spine BMD ≥ 0% and ≥ 3% from baseline at 24 months. Additional secondary end-points were a comparison of the mean percentage change from baseline in biochemical markers of bone turnover (NTX, CTX, BSAP and P1NP) at 24 months between the two treatment groups. Other prespecified analyses included an analysis to determine the proportion of women with BMD increases ≥ 0%, 1%, 2%, 3%, 4% and 5% from baseline at each BMD site at 24 months and an analysis of the proportion of women with BMD losses ≥ 3% at each BMD site. Only data on ≥ 0%, 3% and 5% gain and ≥ 3% loss are shown.

Safety was monitored by investigators, who recorded clinical and laboratory adverse experiences (AEs) during study visits. Patients could report AEs in person or by phone at any time during the study.

Statistical methods

Treatment effect at 6, 12 and 24 months on BMD for all women entering the extension study was assessed by an analysis of variance (ANOVA) on percentage change from baseline using a linear model with terms for treatment and study centre. Treatment differences were estimated by differences in least squares means (LS means) from the ANOVA model, and the 95% confidence intervals (CIs) were calculated. All patients who were enrolled in the 12-month extension who had a baseline BMD, a BMD measurement in the extension, and took at least one dose of study drug in the extension were included in the modified intention-to-treat approach (mITT) analysis. Patients were analysed according to the group to which they were randomised. The percentage of women with BMD increases ≥ 0%, 1%, 2%, 3%, 4% and 5% from baseline at each BMD site at 24 months and the proportion of women with BMD losses ≥ 3% at each BMD site was analysed by a Mantel-Haenszel test stratified by study centre.

The log-transformed fraction of baseline value (calculated by dividing the on-treatment value by the

baseline value and then applying the natural log) was applied to normalise the distribution of changes in biochemical markers before comparisons of alendronate and risedronate were assessed using the same model as in the BMD analyses. For the biochemical marker data at 24 months, the primary analysis was based on a per-protocol (PP) approach, with no data carried forward. All patients or time points with important protocol violations were excluded from the PP analyses. The same cohorts of patients included in the 24-month analyses were used for analyses at 3, 6 and 12 months if they were not protocol violators at the specific time point.

The safety analysis included all patients who received at least one dose of extension study medication in either treatment group. The safety results are cumulative, including both year 1 and year 2 data. Differences in proportions of patients with any AEs, drug-related AEs, serious AEs and discontinuations because of AEs were analysed using Fisher's Exact test. The treatment groups were also compared for the proportion of patients with upper gastrointestinal (UGI) AEs using Fisher's Exact test.

Results

Patient disposition
From the year-1 FACTS cohort of 936 postmenopausal women, 854 women completed the base study and were eligible to enroll in the 1-year extension (Figure 1). Of these 854 eligible women, 798 (93.4%) enrolled in the extension and received at least one dose of study medication. The completion rates for the

extension phase were similar in the two treatment groups (alendronate 95.5%; risedronate 94.4%).

A similar proportion of alendronate-treated and risedronate-treated women were included in the mITT analyses (90.8% vs. 88.6%). All 798 women who received at least one dose of study medication in the extension were included in the safety analysis.

Demographics and baseline characteristics
There were no meaningful differences in baseline characteristics between the alendronate-treated and risedronate-treated women who participated in the extension (Table 1). The demographics of the extension cohort were similar to those of the 936 women in the year 1 study cohort and to the 138 women who were not eligible or chose not to enroll in the extension.

Primary and secondary end-points
Increases from baseline in BMD at month 24 were significantly ($p = 0.002$ for femoral neck, $p < 0.001$ for the other sites) greater in patients treated with alendronate than in those treated with risedronate at all sites measured: the hip trochanter, total hip, femoral neck and lumbar spine (Figure 2A–D). At month 24, the treatment differences were 1.5% (95% CI: 0.7–2.3%) at the trochanter, 1.3% (95% CI: 0.9–1.8%) at the total hip, 1.0% (95% CI: 0.3–1.6%) at the femoral neck and 1.7% (95% CI: 1.1–2.3%) at the lumbar spine. The between-group difference at the hip trochanter was numerically larger than that seen at month 12. The differences increased with time at all sites (Figure 2). The increases in BMD
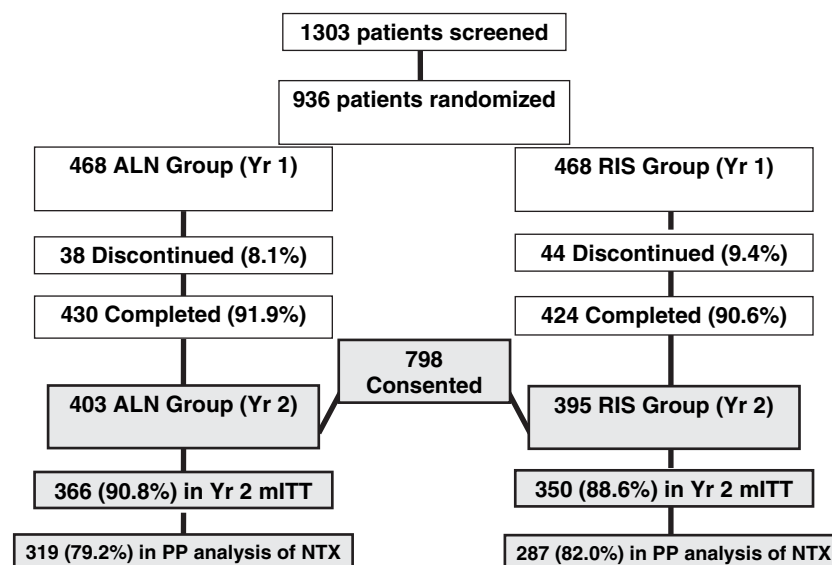

Figure 1 Patient accounting

Table 1 Patient demographics and baseline BMD measurements

Baseline characteristics	ALN 70 mg OW (n = 403)	RIS 35 mg OW (n = 395)	Year 2 cohort (N = 798)	Year 1 cohort (N = 936)	Year 1 patients who did not enter extension (N = 138)
Age (years)	64.3	63.6	63.9	64.1	65.3
Years since menopause	16.8	16.4	16.6	16.8	18.0
Race (% Caucasian)	79.7	78.3	78.3	78.5	79.7
T-score					
Hip trochanter	−1.55	−1.60	−1.58	−1.60	−1.71
Total hip	−1.64	−1.69	−1.67	−1.68	−1.76
Femoral neck	−2.08	−2.14	−2.11	−2.12	−2.15
PA lumbar spine	−2.64	−2.65	−2.65	−2.64	−2.64

BMD, bone mineral density; ALN, alendronate; RIS, risedronate; OW, once weekly; PA, postero-anterior.
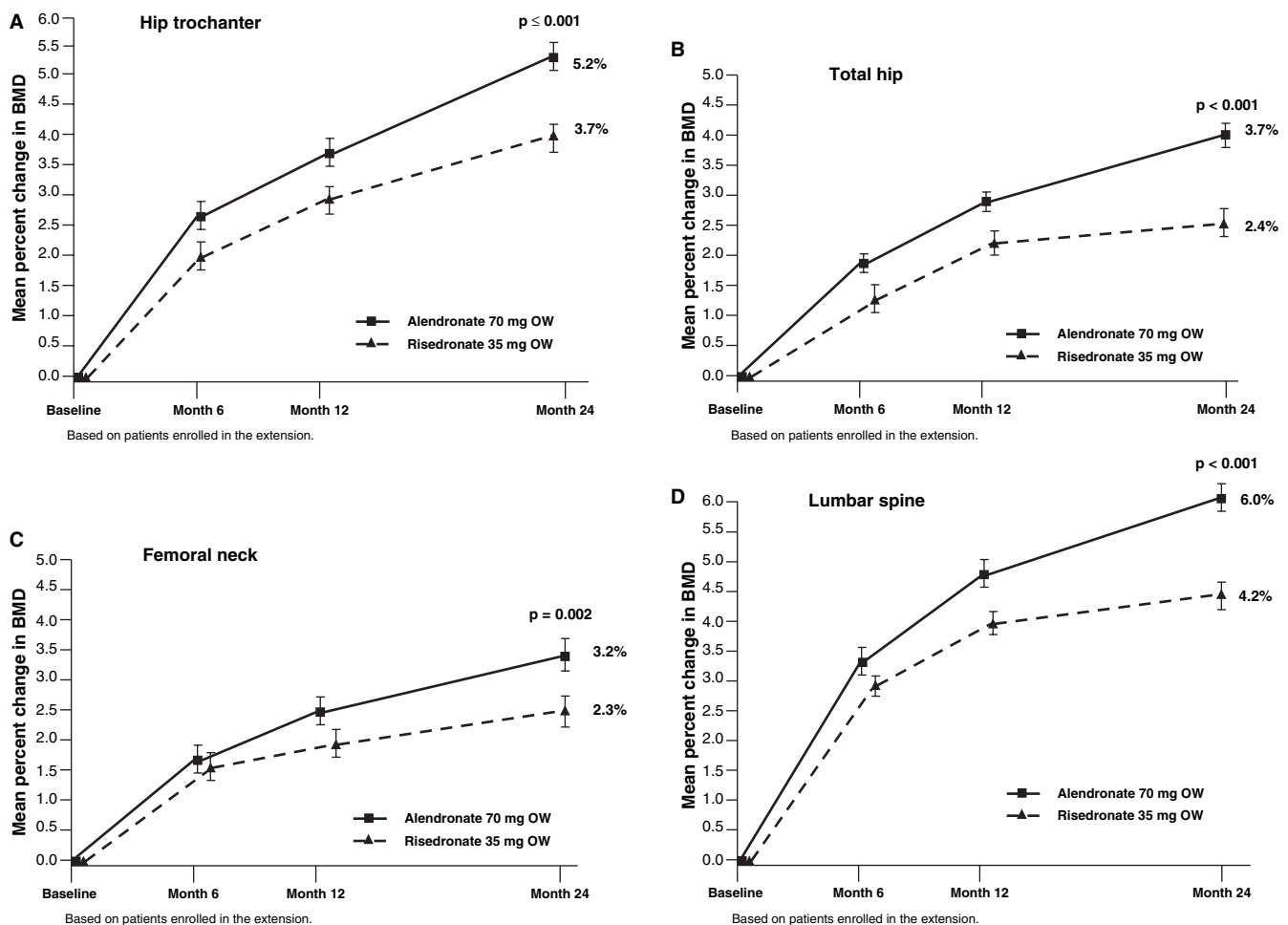
Figure 2 Mean percentage changes in bone mineral density (BMD) from baseline. Mean per cent change from baseline to month 24 ± standard error (modified intention-to-treat approach). (A) Hip trochanter BMD; (B) total hip BMD; (C) femoral neck BMD and (D) lumbar spine BMD

from baseline at all time points were significant for both treatment groups.

Significantly more women treated with alendronate maintained or gained BMD at each of the four sites than those treated with risedronate (Table 2).

Regardless of the level (0%, 1%, 2%, 3%, 4% or 5%) used to categorise gains in BMD, the differences in the proportions between the two treatment groups achieving the respective levels consistently favoured alendronate.

Table 2 Prespecified gains and losses in BMD at 24 months

BMD losses or gains	Hip trochanter		Total hip		Femoral neck		Lumbar spine	
	ALN (N = 366) %	RIS (N = 350) %	ALN (N = 365) %	RIS (N = 351) %	ALN (N = 366) %	RIS (N = 351) %	ALN (N = 365) %	RIS (N = 353) %
≤−3%	4	8	2	4	5	8	1	5
≥ 0%	89	79	91	79	81	71	95	85
≥ 3%	70	53	62	42	52	39	77	61
≥ 5%	52	36	32	21	31	25	56	39

Treatment comparisons (ALN vs. RIS): p ≤ 0.001 for BMD gains at the trochanter, total hip and lumbar spine. For the femoral neck, p = 0.002 for gains ≥ 0%, p = 0.001 for gains ≥ 3% and p = 0.081 for gains ≥ 5%. For losses ≤ −3%, p = 0.006 at the trochanter, p = 0.067 at the total hip, p = 0.145 at the femoral neck and p = 0.004 at the lumbar spine. ALN, alendronate; BMD, bone mineral density; RIS, risedronate.
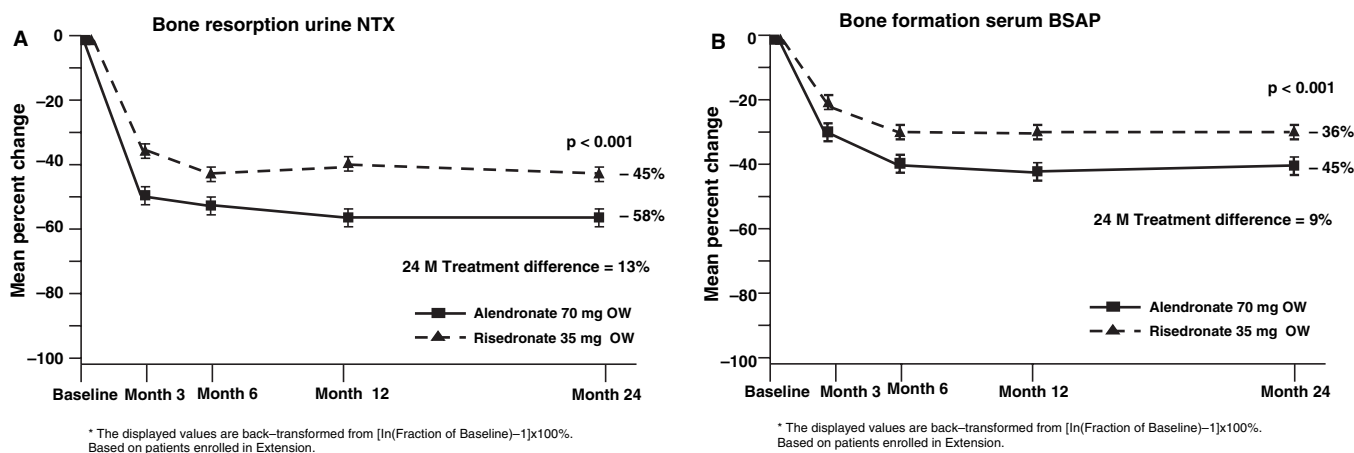
Figure 3 Changes in biochemical markers expressed as mean percentage change from baseline ± SE at 3, 6, 12 and 24 months (per-protocol approach). (A) Urine N-telopeptide of type 1 human collagen (NTX) corrected for creatinine; (B) serum bone-specific alkaline phosphatase (BSAP). p < 0.001 for all time points

Fewer patients treated with alendronate showed a measured decrease in BMD than those treated with risedronate. This was true regardless of the level used to categorise the decrease or the site of BMD measurement (only data on ≥ 3% shown). For example, patients treated with risedronate were two times more likely than patients treated with alendronate to show a decrease of 3% or more depending on the skeletal site; however, the number of patients in either group with BMD decreases was small (Table 2).

Biochemical markers of bone turnover

Both treatments significantly reduced bone resorption, as measured by per cent change from baseline in urine NTX (Figure 3A) and serum CTX. After 24 months of therapy, alendronate reduced NTX and CTX by 58.2% and 69.3%, respectively (CTX data not shown), whereas the corresponding reductions

for risedronate were 45.0% and 44.0%. In both cases, the respective differences between the two treatment groups were significant by as early as 3 months and were maintained at 24 months (p < 0.001).

Alendronate reduced serum levels of the bone formation markers BSAP (Figure 3B) and P1NP after 24 months by 45.1% and 66.4% respectively (P1NP data not shown). The corresponding reductions for risedronate were 36.2% and 51.6%. The differences between the two treatment groups were significant at 24 months (p < 0.001) and at all measured time points from 3 months onward.

Safety

There were no significant differences between treatment groups in the overall rate of clinical AEs at 24 months: 74.7% alendronate-treated and 75.7% risedronate-treated women reported one or more clinical AEs. There were no significant differences

Table 3 Incidence of adverse events (AEs)

Number (%) of patients	Alendronate 70 mg OW (N = 403) n (%)	Risedronate 35 mg OW (N = 395) n (%)
With one or more clinical AE	301 (74.7)	299 (75.7)
With serious AE	42 (10.4)	44 (11.1)
Discontinued because of AE	5 (1.2)	5 (1.3)
Discontinued because of serious AE	3 (0.7)	3 (0.8)
With one or more UGI AE	91 (22.6)	73 (18.5)
With serious UGI AE	3 (0.7)	2 (0.5)
Discontinued because of UGI AE	1 (0.2)	2 (0.5)
Discontinued because of serious UGI AE	0	1 (0.3)
With clinical fractures	23 (5.7)	25 (6.3)

UGI, upper gastrointestinal; OW, once weekly.

between the treatment groups in the incidence of serious AEs (10.4% alendronate, 11.1% risedronate) or discontinuations because of AEs (1.2% alendronate, 1.3% risedronate). Similarly, over 24 months, there were no significant differences in UGI AEs between the two treatment groups (22.6% alendronate, 18.5% risedronate) or in the proportion of women discontinuing because of an UGI AE (0.2% alendronate, 0.5% risedronate; Table 3). The most common UGI AEs reported overall were dyspepsia (alendronate 7.2%, risedronate 5.3%) and nausea (alendronate 5.0%, risedronate 4.8%). The differences between the treatment groups were not significant. There were no apparent differences in AE reporting rates during the year 2 extension period compared with the year 1 base study.

Fractures that occurred during the trial, regardless of association with trauma or skeletal site, were reported by investigators as clinical AEs. There was no requirement for central radiographic confirmation or adjudication because fractures were not an efficacy end-point. Over the 24-month treatment period, 26 fractures were reported in 23 (5.7%) alendronate-treated patients (month 0–12: 16 fractures in 14 patients; month 12–24: 10 fractures in nine patients), and 31 fractures were reported in 25 (6.3%) risedronate-treated patients (month 0–12: 16 fractures in 13 patients; month 12–24: 15 fractures in 12 patients).

Discussion

This extension study has demonstrated that the increased BMD and decreased bone markers in alendronate-treated patients compared with those treated with risedronate seen in both this cohort after 12 months of therapy (29) and in a separate US study (28) is maintained throughout a second

12-month treatment period. These continued better changes in surrogate markers of bone strength with alendronate were achieved with a very similar adverse event profile, including UGI AEs.

Although the best method by which to evaluate the relative efficacy and tolerability of two therapies is direct (head-to-head) comparison with fracture as the primary end-point, the large estimated numbers required to show differences in per cent fracture make such trials economically non-viable (24). Using surrogate end-points to compare therapies is therefore the best that can be achieved. The relatively weak relationships between per cent BMD improvement and fracture rate reduction at the spine (30) and non-spine (3) sites and the somewhat stronger relationships between reduction in bone turnover markers, both with risedronate (31) and alendronate, (32) and per cent fracture reduction give some justification for the use of the surrogate end-points examined in this study.

Accordingly, it is worthwhile considering how else these data may be used in a clinical setting. Although there is no universal agreement on the need for monitoring the effectiveness of treatment either with repeated BMD assessment (33) or repeated measures of bone markers, (34) there is an increasing understanding of the concept of the use of least significant change (LSC) when considering the time interval for repeating a test. Significant BMD changes exceeding the LSC threshold, calculated by the formula $(1.98 \times SD)$ (35), are much more likely to occur by 2 years of treatment with alendronate than risedronate. This is demonstrated by the responder analysis (Table 2) where, assuming a LSC at the lumbar spine of 3%, the proportion of patients treated with alendronate in whom clinicians would be able to reassure that a significant improvement had occurred

would be 77% for alendronate and 61% for risedronate. This implies very good precision of < 1.1%, however, which is unlikely in elderly patients due to the effects of fracture and degenerative change (33). The effect of a more realistic precision of 1.8% is shown in the responder analysis for a 5% improvement in LS BMD, and here it can be seen that 56% of alendronate patients could be reassured that their BMD had significantly improved compared with only 39% of risedronate-treated women.

A recent observational study (REAL) (36) of health plan records of women aged ≥ 65 years concluded that risedronate may reduce fracture risk to a greater extent than alendronate. However, as pointed out by Black and Rosen (37), caution must be used when considering conclusions from observational studies of drug therapy. A basic limitation of these kinds of studies is the lack of randomisation, which precludes any direct comparison of efficacy, even with statistical adjustments. Observational studies are not intended to make causal inferences, whereas properly conducted randomised controlled trials can. The current report, although not examining fractures, did compare the effects of both alendronate and risedronate on accepted surrogate markers of bone strength in postmenopausal women with osteoporosis in a rigorous controlled head-to-head trial and showed significantly greater increases in BMD and decreases in levels of bone turnover markers with alendronate than with risedronate.

Despite concerns about the relative safety and particularly the GI tolerability of alendronate compared with risedronate (38–43), both drugs were well tolerated and resulted in very few discontinuations because of severe AEs arising either in the GI tract or elsewhere. Tolerability of oral medications for osteoporosis has been a concern, and there has been a perception that risedronate may be better tolerated than alendronate. This study shows that there was no significant difference in tolerability overall (as measured by clinical AEs, serious AEs and discontinuation because of AEs), nor in UGI tolerability between the two therapies.

The main limitation of this study is that the size of the study precluded any chance of demonstrating a significant difference in fracture rates between the two treatments. The study was not powered to demonstrate such a difference and, in addition, no vertebral radiographs were taken during the study that could have been used to determine morphometric vertebral fracture rates in the two treatment arms.

In conclusion, in this direct head-to-head study of alendronate and risedronate given weekly at the indicated dose for postmenopausal osteoporosis, alendronate was superior in its efficacy (as measured by BMD and biochemical bone turnover markers) vs. risedronate. Osteoporosis is a disorder that often leads to significant morbidity when untreated. Choosing a medication that is both well tolerated and has shown efficacy in both placebo-controlled trials and comparative studies is important. Physicians should take the results from this study into account when prescribing an antiresorptive agent for the treatment of their postmenopausal patients with osteoporosis.

Author contributions

Acknowledgements and funding

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