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Original article

Effectiveness of monthly intravenous ibandronate injections in a real-world setting: Subgroup analysis of a postmarketing observational study

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ABSTRACT

Objectives: The favorable safety and consistent effectiveness of monthly intravenous (IV) ibandronate injections was demonstrated in a prospective, postmarketing, observational study in Japanese patients with osteoporosis. Here, we present subgroup analyses from the study.
Methods: Lumbar spine (L2–4) bone mineral density (BMD) gains were assessed in the following subgroups: aged <75 or ≥75 years, absence or presence of vertebral fractures, previous bisphosphonate (BP) treatment, and concomitant versus naïve osteoporosis drug treatment. The cumulative incidence of fractures and relative change in bone turnover markers were also examined.
Results: Of 1062 enrolled patients, 1025 received monthly IV ibandronate 1 mg and were assessed for 12 months. BMD gains with ibandronate were comparable, irrespective of older age or prevalent fractures. Overall, 515 patients (50.2%) had previously received osteoporosis treatment; of these, 166 (16.1%) received other BPs. Mean BMD changes were 3.69% (95% confidence interval [CI], 0.89%–6.50%) in patients previously treated with other BPs, and 4.26% (95% CI, 2.88%–5.64%) in patients who had not received prior osteoporosis treatment. Among the 510 patients (49.7%) concomitantly prescribed active vitamin D drugs, mean BMD changes were 5.74% (95% CI, 2.53%–8.95%) with eldecalcitol versus 3.54% (95% CI, 1.98%–5.10%) with ibandronate alone. The lowest fracture incidence was observed with the combination of ibandronate and eldecalcitol, but differences between the subgroups were not statistically significant.
Conclusions: Monthly IV ibandronate demonstrated comparable BMD gains in the patient subgroups analyzed. Concomitant use of ibandronate with eldecalcitol showed a trend of higher BMD gains and lower fracture incidence than ibandronate alone.

1. Introduction

With the exception of Japan, 2 formulations of ibandronate have been commercially available in Western countries for more than a decade, quarterly intravenous (IV) 3 mg injection and monthly oral 150 mg tablet. Meta-analyses of clinical studies have confirmed the efficacy of these ibandronate regimens in significantly reducing the risk of vertebral, nonvertebral, and clinical fractures [1–7].

Bisphosphonates (BPs) are the standard first-line treatment of choice for osteoporosis in Western countries and in Japan. Patients' preference for once-monthly intermittent BP dosing regimens over more frequent administration has been documented [8]. To meet the medical preferences of Japanese patients, 2 monthly formulations of ibandronate, monthly bolus IV 1 mg injection and monthly oral 100 mg tablet, were made commercially available in Japan. In the MOVER (MOnthly intraVenous ibandronatE versus daily oral Risedronate) registration study, the noninferiority of monthly IV ibandronate 1 mg to oral risedronate with respect to vertebral fracture risk reduction was demonstrated [9,10]. Rather, monthly IV

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ibandronate treatment reduced the incidence of both vertebral and nonvertebral fractures compared with risedronate [9,11]. The availability of monthly IV ibandronate injections has improved treatment adherence in Japanese patients with osteoporosis, which may ultimately enhance clinical benefit [12,13].

A number of postlaunch pharmacovigilance actions must be taken to ensure the safety of monthly IV ibandronate. As one such action, we conducted a prospective, postmarketing and observational study in Japanese women and men with osteoporosis; data for the first 12 months' of treatment were published previously [14]. From these results, the favorable safety and consistent effectiveness of monthly IV ibandronate was confirmed in a real-world setting.

To accumulate further evidence for the effectiveness of ibandronate in a real-world setting, and to consider personalized treatment options in more detail, we performed subgroup analyses of the postmarketing study.

2. Methods

2.1. Study design and population

The patient subgroups used in this analysis originated from a prospective, postmarketing, observational study (BON1301) [14], where the safety and effectiveness of monthly IV ibandronate 1 mg was examined in Japanese women and men with osteoporosis in a real-world setting. Patients were recruited from 257 hospitals and clinics including departments of orthopedic surgery and internal medicine.

Eligible patients were diagnosed according to the diagnostic criteria of primary osteoporosis in Japan [15] and registered for the study (UMIN-CTR Clinical Trial number: UMIN000013412). Primary osteoporosis is defined by the World Health Organization as a bone mineral density (BMD) of T-score reduced by −2.5 standard deviations or more, whereas in Japan it is defined as a BMD of Young Adult Mean reduced to less than or equal to 70%. Patients were excluded from the study if they had any contraindications to ibandronate treatment, as described in the drug label, or if they had been treated with the drug before participating in the study. All patients received monthly ibandronate 1 mg injections (Bonviva, Chugai Pharmaceutical Co., Ltd., Tokyo, Japan), with an observation period of 12 months for women and 36 months for men. Data collection for the male study population is still ongoing.

The study was conducted in accordance with good postmarketing study practice regulations from the Ministry of Health, Labour, and Welfare in Japan. According to the regulations of individual institutions, the study protocol was reviewed and approved by the ethics committee and written or verbal informed consent was obtained.

2.2. Subgroup analysis

We assessed lumbar spine (L2–4) BMD gains in the following patient subgroups: younger versus older age (<75 or ≥75 years); absence versus presence of vertebral fractures; previous treatment with other BPs (alendronate, minodronate, or risedronate) or osteoporosis drug treatment other than BPs within 6 months prior to the start of the study; and treatment along with vitamin D drug (eldecalcitol, alfacalcidol, or calcitriol) versus without any vitamin D drug. In addition, we examined changes in the levels of serum tartrate-resistant acid phosphatase-5b (TRACP-5b) as a bone turnover marker, and the cumulative incidences of nonvertebral and clinical fractures.

2.3. Schedule of assessments

BMD gains were measured at baseline, 6, and 12 months using dual-energy X-ray absorptiometry. Changes from baseline in TRACP-5b levels were measured at baseline, 6, and 12 months in the subgroup analysis. The date and location of nontraumatic nonvertebral fractures and clinical fractures were recorded and assessed according to radiographs.

2.4. Statistical analyses

Changes from baseline in BMD and TRACP-5b, with 95% confidence intervals (CIs), were recorded, and fracture incidence rates and corresponding 95% CIs were calculated. Cumulative fracture

Table 1
Baseline patient characteristics (n = 1025).

Characteristic	Value
Women	887 (86.5)
Age, yr	77.1 ± 9.0
<75	353 (34.4)
≥75	672 (65.5)
Weight, kg	49.1 ± 8.7
Women only	48.1 ± 8.3
Height, cm	150.2 ± 8.0
Women only	148.7 ± 7.0
Prevalent nonvertebral fractures	
Yes	57 (5.5)
No	968 (94.4)
Vertebral fractures	
1	141 (13.7)
>1	147 (14.3)
Previous osteoporosis drug treatment[a]	
Yes	515 (50.2)
Bisphosphonates	166 (16.1)
Active vitamin D agents	345 (33.6)
Selective estrogen receptor modulators	51 (4.9)
Teriparatide	46 (4.4)
No	510 (49.7)
Concomitant use of osteoporosis drugs	
Yes	569 (55.5)
Active vitamin D agents	510 (49.7)
Eldecalcitol	370 (36.0)
Others	140 (13.6)
Calcium agents	60 (5.8)
No	456 (44.4)
TRACP-5b, mU/dL	459.5 ± 215.3
Serum NTX, nmol BCE/L	22.9 ± 18.3
P1NP, μg/L	56.3 ± 34.8
BAP, μg/L	17.1 ± 10.0
Serum calcium adjusted, mg/dL	9.1 ± 0.5
eGFR, mL/min/1.73m^2	67.64 ± 20.62
Bone mineral density by subgroup, g/cm^2	
No prior treatment (n = 109)	0.743 ± 0.141
Prior bisphosphonates (n = 48)	0.776 ± 0.173
Prior other osteoporosis drug treatment (n = 91)	0.788 ± 0.182
No concomitant treatment (n = 95)	0.754 ± 0.156
Concomitant treatment with eldecalcitol (n = 94)	0.768 ± 0.180
Concomitant treatment with other vitamin D agents (n = 47)	0.779 ± 0.151
TRACP-5b value by subgroup, mU/dL	
No prior treatment (n = 92)	522.0 ± 193.8
Prior bisphosphonates (n = 27)	404.5 ± 242.8
Prior other osteoporosis drug treatment (n = 55)	477.0 ± 232.0
No concomitant treatment (n = 68)	510.3 ± 194.3
Concomitant treatment with eldecalcitol (n = 65)	457.8 ± 198.2
Concomitant treatment with other vitamin D agents (n = 27)	502.9 ± 278.6

Values are presented as number (%) or mean ± standard deviation.
TRACP-5b, tartrate-resistant acid phosphatase-5b; NTX, serum N-telopeptide of type 1 collagen; BCE, bone collagen equivalent; P1NP, procollagen type 1 N-terminal propeptide; BAP, bone-specific alkaline phosphatase; eGFR, estimated glomerular filtration rate.
Modified from Takeuchi Y et al. Osteoporos Sarcopenia 2018; 4:22-8 [14].
[a] Within 6 months of the start of the study.

rates were assessed using Kaplan-Meier methodology. All statistical analyses were conducted using SAS System Release 9.2 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Patient disposition and baseline characteristics

Of 1062 patients who were enrolled, 1025 patients (887 women and 138 men) were treated and assessed. The clinical report records were not collected from 22 patients, and the safety assessment was not available in a further 15 patients. Baseline patient characteristics are summarized in Table 1 [14]. Overall, 50.2% of patients had received other osteoporosis agents prior to ibandronate and 55.5% of patients were receiving other osteoporosis agents (active vitamin D agents, 49.7%; calcium agents, 5.8%) concomitantly with ibandronate.

3.2. Bone mineral density

In the overall study population, the mean change in L2–4 BMD gains was 3.20% (n = 183; 95% CI, 2.40%–4.01%) at 6 months and 4.84% (n = 187; 95% CI, 3.47%–6.21%) at 12 months from baseline (n = 248) [14].

In patients aged <75 versus ≥75 years, L2–4 BMD gains at 12 months were 4.30% (95% CI, 2.82%–5.77%) and 5.24% (95% CI, 3.12%–7.36%), respectively (Fig. 1A). L2–4 BMD gains at 12 months were 5.75% (95% CI, 3.95%–7.56%) and 5.21% (95% CI, 2.42%–8.00%), respectively, in patients with versus without prevalent vertebral fractures (Fig. 1B).

A total of 515 patients (50.2%) had received previous osteoporosis drug treatment within 6 months of the start of the study (Table 1). Of these, 166 patients (16.1%) were treated with other BPs. The mean BMD change at L2–4 in patients who had not received prior osteoporosis treatment was 4.26% (95% CI, 2.88%–5.64%) compared with 3.69% (95% CI, 0.89%–6.50%) in patients previously treated with other BPs, and 6.12% (95% CI, 3.13%–9.11%) in patients receiving other prior osteoporosis treatment at 12 months from baseline (Fig. 2A).

Active vitamin D drugs had been concomitantly prescribed to 510 patients (49.7%) (Table 1). Mean L2–4 BMD changes were 3.54% (95% CI, 1.98%–5.10%) in patients treated with ibandronate alone, 5.74% (95% CI, 2.53%–8.95%) in patients treated concomitantly with eldecalcitol, and 5.78% (95% CI, 3.65%–7.86%) in patients receiving concomitant alfacalcidol or calcitriol at 12 months from baseline (Fig. 3A).

3.3. Bone turnover markers

For the subgroup of patients who had not received prior osteoporosis treatment, mean changes in TRACP-5b levels were −32.86% (95% CI, −39.85% to −25.87%) at 6 months and −32.42% (95% CI, −42.98% to −21.86%) at 12 months from baseline (Fig. 2B). Mean changes in TRACP-5b levels at 6 and 12 months, respectively, were −15.40% (95% CI, −30.51% to −0.30%) and −11.83% (95% CI, −28.46% to 4.80%) for patients who were treated with other BPs, and −32.56% (95% CI, −40.07% to −25.05%) and −40.02% (95% CI, −48.48% to −31.56%) for patients who were treated with other osteoporosis drugs (Fig. 2B).

With respect to vitamin D drug treatment, mean changes in TRACP-5b levels were −25.42% (95% CI, −33.39% to −17.45%) at 6 months and −27.52% (95% CI, −41.03% to −14.01%) at 12 months from baseline for patients who were treated with ibandronate alone, −37.93% (95% CI, −46.14% to −29.72%) and −36.74% (95% CI, −46.83% to −26.65%), respectively, for patients who were concomitantly treated with eldecalcitol, and −29.33% (95%

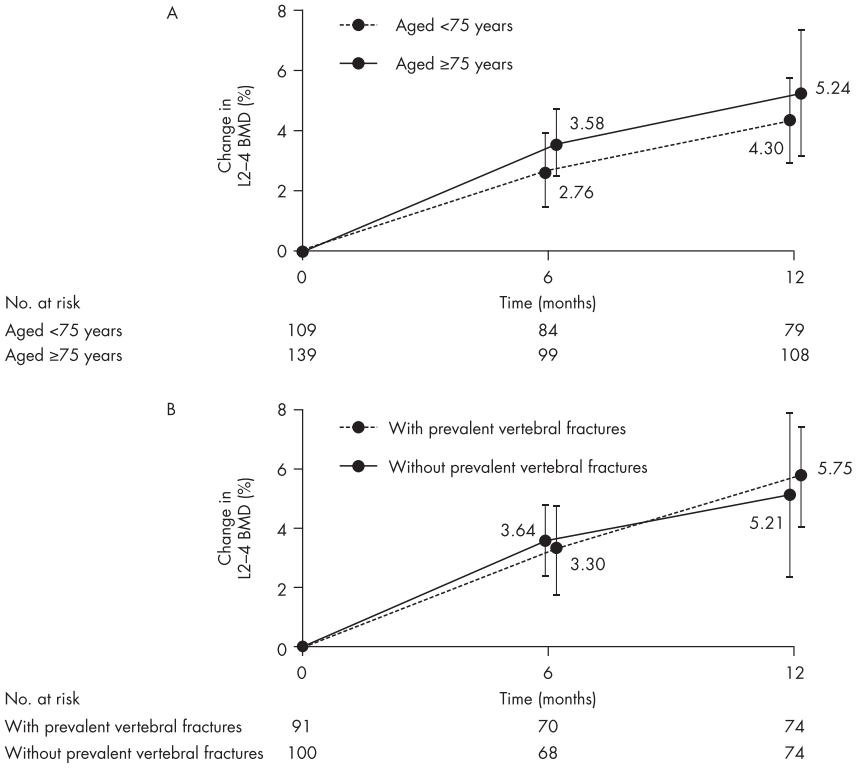

Fig. 1. Mean relative change in lumbar spine (L2–4) bone mineral density (BMD) from baseline to 12 months (with 95% confidence interval) in: (A) patients aged <75 versus ≥75 years; and (B) patients with versus without prevalent vertebral fractures.

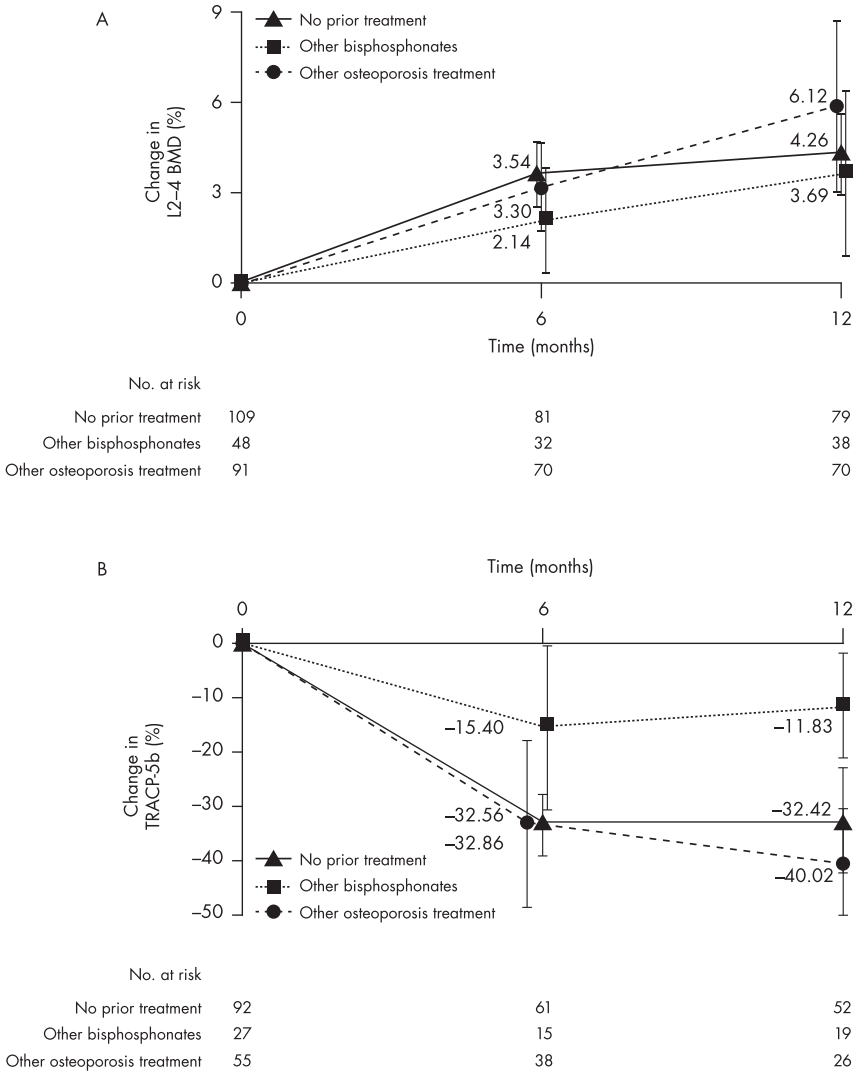

Fig. 2. Mean relative change in: (A) lumbar spine (L2–4) bone mineral density (BMD) and (B) tartrate-resistant acid phosphatase-5b (TRACP-5b) levels from baseline to 12 months (with 95% confidence intervals) in patient subgroups receiving no prior treatment, other bisphosphonates, or other osteoporosis treatment.

CI, −41.08% to −17.58%) and −23.67% (95% CI, −36.83% to −10.51%), respectively, for patients who were treated with other active vitamin D drugs (Fig. 3B).

3.4. Fracture incidence

In the overall study population, cumulative nonvertebral fracture incidences were 0.95% (95% CI, 0.47%–1.89%) at 6 months and 1.81% (95% CI, 1.07%–3.05%) at 12 months, while corresponding clinical fracture incidences were 1.64% (95% CI, 0.97%–2.75%) and 3.47% (95% CI, 2.39%–5.04%), respectively [14].

Analyses based on prior osteoporosis drug treatment revealed that the cumulative incidences of nonvertebral fractures at 6 and 12 months, respectively, were 0.62% (95% CI, 0.08%–4.38%) and 1.41% (95% CI, 0.35%–5.57%) in patients who had received other BPs (n = 175), 1.36% (95% CI, 0.51%–3.60%) and 2.21% (95% CI, 0.99%–4.88%) in patients with other osteoporosis pretreatment (n = 346), and 0.77% (95% CI, 0.25%–2.38%) and 1.67% (95% CI, 0.75%–3.70%) in patients without pretreatment (n = 504). At 6 and 12 months, respectively, the cumulative incidences of clinical fractures by prior osteoporosis drug treatment were 0.62% (95% CI, 0.08%–4.35%) and 2.15% (95% CI, 0.69%–6.56%) in patients with BP pretreatment (n = 175), 2.07% (95% CI, 0.93%–4.55%) and 4.22% (95% CI, 2.35%–7.52%) in patients with other osteoporosis pretreatment (n = 346), and 1.71% (95% CI, 0.81%–3.57%) and 3.70% (95% CI, 2.20%–6.19%) in patients without pretreatment (n = 504). At 6 and 12 months, respectively, the incidences of vertebral fractures by prior osteoporosis drug treatment were not observed in patients with BP pretreatment (n = 78), 0.68% (95% CI, 0.09%–4.76%) and 3.32% (95% CI, 1.25%–8.65%) in patients with other osteoporosis pretreatment (n = 146), and 2.88% (95% CI, 1.30%–6.30%) and 4.63% (95% CI, 2.43%–8.75%) in patients without pretreatment (n = 208).

With respect to vitamin D drug treatment, the cumulative incidence of nonvertebral fractures at 6 and 12 months from baseline, respectively, was 0.35% (95% CI, 0.04%–2.47%) and 0.35% (95% CI, 0.04%–2.47%) in patients treated concomitantly with eldecalcitol (n = 370), 0.82% (95% CI, 0.11%–5.72%) and 3.85% (95% CI, 1.45%–10.01%) in patients concomitantly treated with other active vitamin D drugs (n = 140), and 1.61% (95% CI, 0.72%–3.56%) and 2.55% (95% CI, 1.33%–4.87%) in patients treated with ibandronate alone (n = 456; Fig. 4). The cumulative incidences of clinical fractures at 6 and 12 months, respectively, by vitamin D drug treatment, were 1.01% (95% CI, 0.32%–3.11%) and 2.19% (95% CI, 0.99%–4.84%) in patients concomitantly treated with eldecalcitol

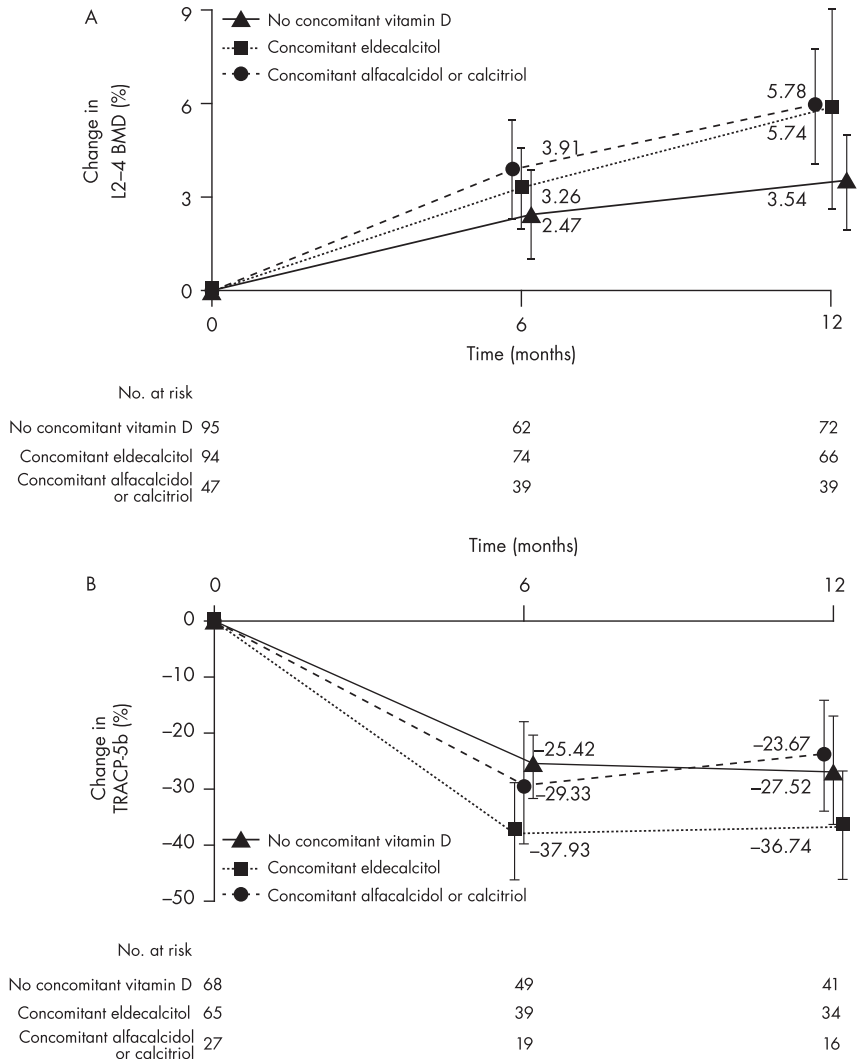

Fig. 3. Mean relative change in: (A) lumbar spine (L2–4) bone mineral density (BMD) and (B) tartrate-resistant acid phosphatase-5b (TRACP-5b) levels from baseline to 12 months (with 95% confidence intervals) in patient subgroups receiving no concomitant vitamin D, concomitant eldecalcitol, or concomitant alfacalcidol or calcitriol.

(n = 370), 1.65% (95% CI, 0.41%–6.44%) and 5.67% (95% CI, 2.57%–12.25%) in patients concomitantly treated with other active vitamin D agents (n = 140), and 2.36% (95% CI, 1.23%–4.50%) and 4.52% (95% CI, 2.70%–7.30%) in patients treated with ibandronate alone (n = 456; Fig. 5). The incidences of vertebral fractures at 6 and 12 months, respectively, by vitamin D drug treatment, were 0.64% (95% CI, 0.09%–4.49%) and 2.23% (95% CI, 0.72%–6.80%) in patients concomitantly treated with eldecalcitol (n = 155), not observed and 1.75% (95% CI, 0.24%–11.80%) in patients concomitantly treated with other active vitamin D agents (n = 71), and 3.29% (95% CI, 1.49%–7.19%) and 5.33% (95% CI, 2.80%–10.05%) in patients treated with ibandronate alone (n = 182).

4. Discussion

We performed subgroup analyses of patients from a post-marketing, observational study to examine the effectiveness of monthly IV ibandronate in a Japanese real-world setting. Our results demonstrated comparable BMD gains in patient subgroups defined by prior other BP or osteoporosis treatments, age, and presence or absence of vertebral fractures. Concomitant use of ibandronate and active vitamin D drugs resulted in greater BMD gains than ibandronate alone, but no differences were observed among the individual vitamin D drugs. Nevertheless, the lowest fracture incidence was seen with the coadministration of ibandronate and eldecalcitol.

We first examined the effectiveness of IV ibandronate in patients aged ≥75 years, which may impact disease stage, as well as in patients with prevalent vertebral fractures. We previously reported that BMD gains at all sites (lumbar spine, femoral neck, and total hip) were substantial and significantly improved over baseline values with monthly IV ibandronate treatment in the original study [14]. The effect of monthly ibandronate in high-risk patients was examined in the MOVER and MOVEST (Monthly Oral VErsus inravenouS ibandronaTe) studies, which reported similar BMD gains [9,16]. In the current subgroup analysis, BMD gains with IV ibandronate were comparable, irrespective of older age or prevalent fractures. Similar findings with respect to older age and prevalent fractures were reported with both IV and oral ibandronate in the MOVER study [17]. Our data reproduce the efficacy of IV ibandronate in daily practice, and highlight its potential as a useful treatment option for patients with different clinical characteristics.

BPs are an established first-line therapy for patients with osteoporosis in Japan. Thus, the influence of BP treatment history and

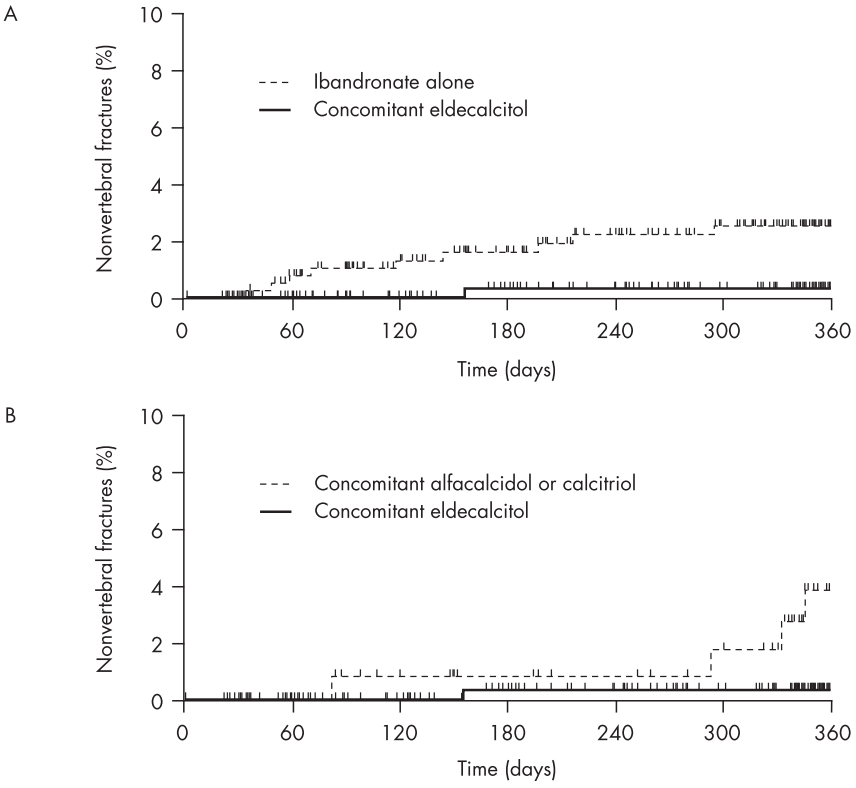

Fig. 4. Nonvertebral fracture incidence according to vitamin D drug treatment: (A) ibandronate alone versus ibandronate with concomitant eldecalcitol; (B) concomitant alfacalcidol or calcitriol versus concomitant eldecalcitol.

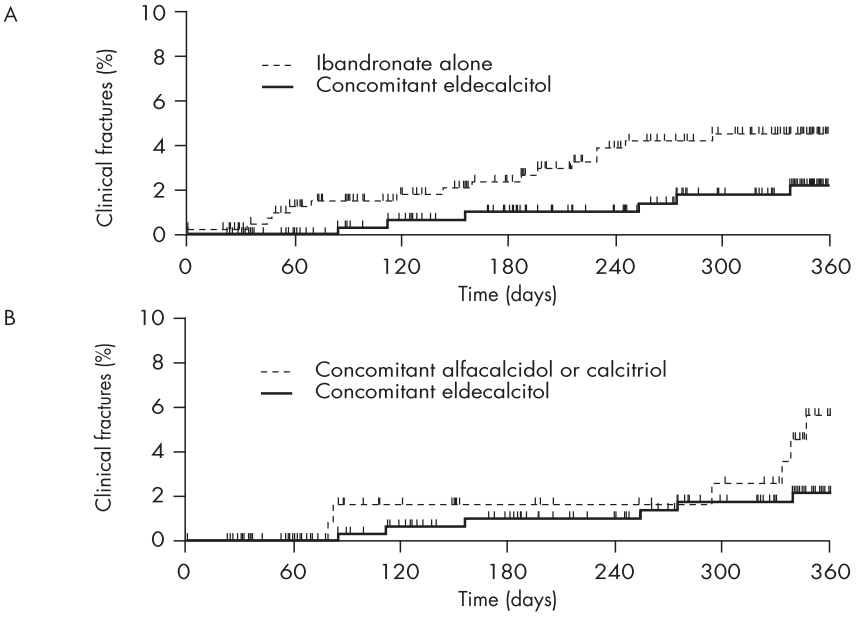

Fig. 5. Clinical fracture incidence according to vitamin D drug treatment: (A) ibandronate alone versus ibandronate with concomitant eldecalcitol; (B) concomitant alfacalcidol or calcitriol versus concomitant eldecalcitol.

prior osteoporosis drug treatment history other than BPs on the effectiveness of subsequent medications is an important parameter to investigate. In our study, approximately half of all patients had received previous osteoporosis drug treatment. BMD gains in patients who had been pretreated with other BPs were observed, although they were lower than in patients without prior osteoporosis therapy. It is possible that switching to IV ibandronate from other BPs resulted in these additional BMD gains. Since prior use of other BPs had already produced a reduction in TRACP-5b levels, the effect observed when switching to IV ibandronate was smaller than that seen without previous osteoporosis drug treatment. BMD gains across each of the patient subgroups were almost

comparable, thus, the incidences of nonvertebral and clinical fractures were also considered to be comparable. The fact that switching to IV ibandronate could enhance BMD gains, means that switching to IV ibandronate from existing oral BPs would be a good long-term treatment strategy for patients. The incidences of nonvertebral and clinical fractures appeared to be slightly higher in patients receiving other osteoporosis pretreatment compared with the other subgroups; the reason for this phenomenon is difficult to explain. However, it is reasonable to assume that there were no clear relationships between BMD gain and/or TRACP-5b decrease and fracture incidence, because only a few patients in each subgroup underwent DXA analysis and/or TRACP-5b measurements. Switching to IV ibandronate could be one treatment option, although patients would need to visit clinics or hospitals each month to receive treatment.

Concerning the concomitant use of osteoporosis drugs, active vitamin D drugs (eldecalcitol, alfacalcidol, calcitriol) were prescribed to 510 patients (49.7%) in addition to IV ibandronate. Of these, 370 patients were treated with eldecalcitol, which has been prescribed most frequently in Japan. Concomitant use of eldecalcitol or other active vitamin D drugs produced greater BMD gains than treatment with ibandronate alone, but its efficacy was comparable among active vitamin D analogs in this study. Nevertheless, the reduction in TRACP-5b levels observed with eldecalcitol was more pronounced than that seen with other active vitamin D drugs. Since eldecalcitol has been commercially available since 2011, its penetration and popularity for osteoporosis treatment has been growing in Japan. Consequently, the combined use of existing BPs and eldecalcitol has become much more widespread in Japan [18]. Among the existing BPs, IV ibandronate administered concomitantly with eldecalcitol has shown the highest BMD gains in daily practice [12,13], but the effectiveness of the combined use of the 2 drugs on fracture risk reduction has not yet been examined. As this was a real-world study, there was no control arm, thus, it is difficult to evaluate the efficacy of the combination regimen on fracture risk reduction. However, our analysis revealed that the lowest incidence of nonvertebral and clinical fractures was seen with the concomitant use of ibandronate and eldecalcitol, although differences between the subgroups were not statistically significant. In a *post hoc* analysis of a randomized, double-blind study, a marked reduction in the incidence of nonvertebral wrist fractures was observed with eldecalcitol compared with alfacalcidol at 36 months (1.1% vs. 3.6%; hazard ratio, 0.29; 95% CI, 0.11%–0.77%) [19]. In the current analysis, only one humerus fracture was reported in patients treated with ibandronate alone. Due to the low fracture incidence rates in each subgroup, these results should be interpreted with caution. Nevertheless, this is the first study to report that the combined use of ibandronate and eldecalcitol produced better fracture risk reduction than ibandronate alone. As the relationship between BMD gains and fracture risk reduction with ibandronate has been reported previously [20,21], substantial BMD gains at all sites in the original study could support the idea that IV ibandronate is efficacious in fracture risk reduction. The relationship between BMD gains and fracture risk reduction with eldecalcitol is rather poor. Thus, it is possible that antifracture effects of eldecalcitol are largely independent of BMD gain. The additive effect on BMD increase by the combined use of ibandronate with eldecalcitol was noted in this current analysis, and its mechanism of effect on fracture risk reduction should be investigated further.

Acute phase reactions, which are commonly experienced following the first administration of intermittent nitrogen-containing BP such as monthly IV ibandronate, were reported in 21 patients (2.04%) in the study [14]. Of these, 6 patients were concomitantly treated with eldecalcitol, 3 patients were concomitantly treated with alfacalcidol, and 12 patients were treated with ibandronate alone. All 21 patients experienced mild-to-moderate transient symptoms [14], and, moreover, there was no specific symptom in patients concomitantly treated with eldecalcitol or alfacalcidol. Increases in serum or urine calcium is a well-established adverse drug reaction (ADR) with eldecalcitol. There was one case reported as hypercalcemia during our study. The case occurred after 9 months of concomitant treatment with eldecalcitol, however, the patient's serum calcium level returned to within the normal range at the next assessment without intervention. Clinical evidence for the use of combination therapy in osteoporosis has been published [22]. Indeed, the combination of BPs and active vitamin D drugs has been gaining acceptability in Japan [12,13]. ADRs should be carefully monitored in daily practice when prescribing a combination of drugs.

There are some limitations to this subgroup analysis. The purpose of the original study was to examine the safety and effectiveness of monthly IV ibandronate in a real-world setting, so only one-third of registered patients had prevalent fractures. Due to the small sample size, such as numbers of fractures of some subgroups, statistical evaluations were not robust. The subgroup analysis was predefined, however, it was exploratory in terms of its ability to differentiate the effectiveness of eldecalcitol from that of other active vitamin D drugs.

5. Conclusions

Monthly IV ibandronate demonstrated comparable BMD gains in the patient subgroups analyzed. Concomitant use of ibandronate with eldecalcitol showed a trend of higher BMD gains and lower fracture incidence than ibandronate alone. The results of the subgroup analysis suggest that monthly IV ibandronate has a positive clinical-benefit profile in a real-world setting, which is supported by a clinical development program.

Conflicts of interest

This registry study was sponsored by Chugai Pharmaceutical Co., Ltd. Y. T. has disclosed that he received research grants from Chugai Pharmaceutical Co., Ltd. and Daiichi-Sankyo Inc., and is a member of the speakers' bureau for Chugai Pharmaceutical Co., Ltd., Daiichi-Sankyo Inc., Teijin Pharma Ltd., and Asahikasei Pharma Corp. J. H., H. K., Y. N., K. M., and C. Y. have disclosed that they are employees of Chugai Pharmaceutical Co., Ltd. No other potential conflict of interest relevant to this article was reported.

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