

Favourable safety profile of once-monthly oral ibandronate in postmenopausal osteoporosis: 1-year results from MOBILE

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SUMMARY

- As for other chronic, asymptomatic conditions, adherence to therapies for postmenopausal osteoporosis is suboptimal.
- Adverse events are a frequently cited reason for treatment withdrawal and contribute to the less than optimal adherence observed with bisphosphonate treatments in postmenopausal osteoporosis.
- An effective oral bisphosphonate that combines good safety and tolerability with less frequent dosing may improve adherence and hence therapeutic outcomes in postmenopausal osteoporosis.
- Ibandronate (Bonviva) is a potent, nitrogen-containing bisphosphonate with proven antifracture efficacy and safety and tolerability similar to placebo when administered orally, either daily or intermittently with a between-dose interval of >2 months.
- In the MOBILE study, once-monthly oral ibandronate regimens (50+50mg [single doses, consecutive days], 100mg or 150mg [single day]) were at least as effective as the daily oral regimen (2.5mg) after 1 year in 1,609 women with postmenopausal osteoporosis.
- Once-monthly oral ibandronate was well tolerated, with no apparent differences between treatment arms in the overall number of adverse events or number of adverse events per body system.
- Withdrawals from the study were also low and comparable across the treatment arms.
- Specifically, no difference was observed in the incidence of upper gastrointestinal (GI) adverse events.
- Once-monthly oral ibandronate has good tolerability, which is similar to a daily dosing regimen that has a tolerability profile similar to placebo.

INTRODUCTION

- Long-term therapeutic adherence to oral bisphosphonates is required for optimal and sustained therapeutic outcomes in postmenopausal osteoporosis.^{1,2}
- However, adherence to current oral regimens is suboptimal,³⁻⁶ compromising therapeutic outcomes.⁷⁻⁹
- In addition to dosing complexity, adverse events are a commonly cited reason for the premature discontinuation of current oral bisphosphonates.^{10,11}
- Well-tolerated agents that can be administered in simplified, less frequent dosing regimens without loss of efficacy may be advantageous in supporting long-term therapeutic outcomes.
- In postmenopausal osteoporosis, ibandronate administered orally either daily or intermittently with an extended between-dose interval has proven antifracture efficacy (3-year vertebral fracture risk reduction: 62% and 50%, respectively) and safety and tolerability similar to placebo.¹²
- In the MOBILE study, once-monthly oral ibandronate regimens (50+50mg, 100mg, 150mg) were at least as effective as the 2.5mg daily oral ibandronate regimen for bone mineral density (BMD) endpoints in 1,609 women with postmenopausal osteoporosis.¹³
- Adverse events and laboratory safety parameters were also monitored throughout the 1-year study period. Here, we summarise the findings of these analyses.

METHODS

Study design

- Multinational, double blind, randomised, phase III, non-inferiority study.
- Women (aged 55–80 years; ≥5 years since menopause [YSM]) with postmenopausal osteoporosis (lumbar spine [L2–L4] BMD T-score <–2.5 and ≥–5).
- Two years' treatment with either 2.5mg daily oral ibandronate or 50+50mg (single doses, consecutive days), 100mg (single day) or 150mg (single day) once-monthly oral ibandronate.

- Study medication was taken immediately after rising and 1 hour before food, non-study medications and fluids other than water.
- Daily oral calcium (500mg) and vitamin D (400IU) were administered.
- Patients were not specifically excluded if they had a history of upper GI disorder, current and controlled dyspeptic symptoms, or if they were receiving concomitant medications with the potential for upper GI irritation.
- Only patients with uncontrolled active or recurrent peptic ulcer disease were excluded.

Safety parameters

- Adverse events were continuously monitored throughout the study, and specifically included upper GI adverse events and symptomatic clinical fractures.

Safety analysis

- The safety analysis involved all patients who received at least one dose of study medication (including those withdrawing prematurely) and had at least one follow-up data point (safety population).
- The frequency and incidence of adverse events was calculated on a per patient basis.

RESULTS

Patient characteristics

- A total of 1,609 women were randomly assigned to one of the four treatment arms.
- Of these women, 1,583 fulfilled the criteria for inclusion in the safety analysis (Table 1).
- The baseline characteristics of the safety population were well balanced across the treatment groups (Table 1).

Table 1. Patient demographics (mean; safety population).

	2.5mg daily IBN (n=395)	50+50mg monthly IBN (n=396)	100mg monthly IBN (n=396)	150mg monthly IBN (n=396)
Age (years)	66	66	66	66
Weight (kg)	64	64	64	64
Height (cm)	157	157	157	158
Body mass index (kg/m ²)	26	26	26	26
YSM (years)	18	19	19	18
History of previous fractures (n, %)	192 (48.9)	183 (46.3)	180 (45.5)	185 (46.7)
Lumbar spine (L2–L4) BMD (g/cm ²)	0.755	0.756	0.756	0.754
Lumbar spine (L2–L4) BMD (T-score)	–3.3	–3.3	–3.3	–3.3
25-OH-D (ng/mL)	25.7	24.4	25.1	24.7

Withdrawals

- Withdrawals from the study were low and comparable across treatment arms, with 49 (12%), 56 (14%) and 52 (13%) patients withdrawing from the 50+50mg, 100mg and 150mg arms, respectively, compared with 60 (15%) from the daily arm.

Overall safety

- Compared with the daily arm, a comparable incidence of adverse events was observed in the once-monthly ibandronate arms (Table 2).

Table 2. Overall summary of safety (n [%]).

	2.5mg daily IBN (n=395)	50+50mg monthly IBN (n=396)	100mg monthly IBN (n=396)	150mg monthly IBN (n=396)
Any adverse event	273 (69.1)	264 (66.7)	268 (67.7)	277 (69.9)
Any drug-related adverse event	119 (30.1)	106 (26.8)	130 (32.8)	129 (32.6)
Any drug-related adverse event leading to withdrawal	29 (7.3)	20 (5.1)	25 (6.3)	23 (5.8)
Any serious adverse event	19 (4.8)	27 (6.8)	31 (7.8)	28 (7.1)
Any drug-related serious adverse event	2 (0.5)	2 (0.5)	2 (0.5)	0
Any drug-related serious adverse event leading to withdrawal	1 (0.3)	1 (0.3)	0	0
Death	1 (0.3)	0	2 (0.5)	1 (0.3)

- The most commonly occurring adverse events (>5%), irrespective of study drug relationship, were dyspepsia, arthralgia, back pain, nausea, diarrhoea and hypertension; no single adverse event had an incidence >9% (Figure 1).

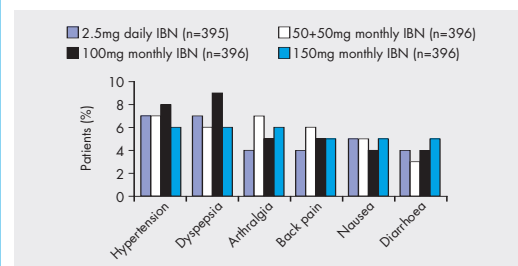


Figure 1. Most commonly occurring (≥5%) adverse events (%; safety population).

- The incidence of serious adverse events was low (Table 2), with the majority of serious adverse events unrelated to study medication.
- The incidence of drug-related adverse events and drug-related serious adverse events was similar across the treatment arms (Table 2).
- Drug-related adverse events and serious adverse events leading to withdrawal were low and balanced across the treatment arms (Table 2).
- In total, four deaths occurred during the study. All were unrelated to treatment (Table 2).

Upper GI adverse events

- The incidence of upper GI adverse events was low and comparable across the treatment arms (Figure 2).

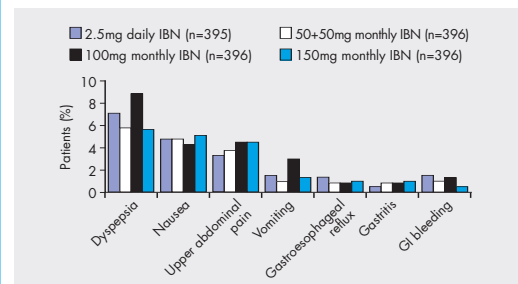


Figure 2. Upper GI adverse events (%; safety population).

- The most commonly reported upper GI adverse events were dyspepsia (5.6–8.8%), nausea (4.3–5.1%) and upper abdominal pain (3.3–4.5%).

Clinical fractures

- After 1 year, no significant differences in the incidence of clinical fractures were observed across the treatment arms.

CONCLUSIONS

- At the studied doses, once-monthly oral ibandronate was well tolerated, with a similar safety profile to a daily oral ibandronate regimen that has previously shown tolerability similar to placebo.
- These results are consistent with previously reported favourable safety findings for oral ibandronate in postmenopausal osteoporosis.¹²
- When combined with the efficacy findings from the MOBILE study, these data strongly indicate that once-monthly oral ibandronate will provide an effective and well tolerated alternative to current daily and weekly oral bisphosphonates in postmenopausal osteoporosis.

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