

Oral ibandronate (150mg) continues to be effective and well tolerated when administered monthly: the MOBILE study long-term extension

Stakkestad JA,¹ Lorenc R,² Czerwinski E,³ Sedarati F,⁴ Neate C,⁵ Reginster J-Y⁶

¹CECOR AS, Haugesund, Norway; ²The Children's Memorial Institute, Warsaw, Poland; ³Krakow Medical Centre, Krakow, Poland; ⁴Hoffmann-La Roche Inc., Nutley, New Jersey, USA; ⁵Roche Products Ltd, Welwyn Garden City, UK; ⁶University of Liège, Liège, Belgium

SUMMARY

- In the Monthly Oral Ibandronate In LadiEs (MOBILE) study, monthly oral ibandronate (Bonviva[®]) (50+50mg, 100mg and 150mg doses) was proven to be at least as effective as the daily oral regimen (2.5mg; vertebral fracture risk reduction 62%, p=0.0001¹ for increasing bone mineral density (BMD)).^{2,3}
- In the MOBILE long-term extension (LTE) study, participating subjects who received either the 100mg or 150mg monthly regimen in the MOBILE study are continuing with their medication for an additional 3 years, while participating subjects who received the 2.5mg daily or 50+50mg monthly regimen have been re-randomised to receive either the 100mg or 150mg regimen.
- After the first year of the LTE a pooled analysis was conducted for patients who received 100mg (n=173) or 150mg (n=168 for lumbar spine, n=169 for hip) oral ibandronate throughout MOBILE and MOBILE LTE (i.e. 3 years of continuous treatment). ITT results are presented throughout for BMD and serum CTX (sCTX) analyses.
- The post-hoc, pooled analysis over 3 years, showed consistent lumbar spine BMD increases from MOBILE study baseline: 7.6% (150mg) and 6.4% (100mg; p<0.0001 for both). Total hip BMD also significantly increased (4.1% and 3.4%, respectively; p<0.0001).
- Median sCTX concentrations remained within the premenopausal range after 3 years and were reduced by 52.0% (100mg arm) and 64.9% (150mg arm) compared with the MOBILE study baseline.
- Monthly ibandronate continued to demonstrate good tolerability, with no meaningful difference between the two treatment arms in terms of overall incidence of adverse events, treatment-related adverse events or upper gastrointestinal (GI) adverse events.
- Monthly oral ibandronate 150mg provides consistent gains in BMD after 3 years of treatment (2 years in MOBILE plus 1 year in MOBILE LTE) with a tolerability profile similar to the daily regimen.

INTRODUCTION

- Bone quality and bone mineral content are key components of bone strength. In MOBILE,^{2,3} monthly oral ibandronate provided superior increases in lumbar spine BMD compared with the daily regimen, which has proven antifracture efficacy (vertebral fracture risk reduction 62%, p=0.0001).¹ BMD gains are associated with fracture risk reduction.⁴
- Monthly ibandronate was well tolerated with a tolerability profile similar to that of the daily regimen, which has a tolerability profile similar to placebo.¹
- The efficacy and safety of 100mg and 150mg monthly ibandronate following the 2-year MOBILE study are being further investigated in a 3-year extension study (MOBILE LTE).
- Compared with BMD at the 2-year endpoint, additional gains in lumbar spine BMD of 1.1% and 1.5% were observed in the 100mg and 150mg arms after the first year of MOBILE LTE (ITT population). Total hip BMD increased by an additional 0.3% over the first year of the LTE with the 150mg regimen (-0.1% for the 100mg dose).²
- Here results are shown from a post-hoc, pooled analysis of data for patients who received 100mg and 150mg during MOBILE (years 1 and 2), and then continued on the same dosing in the first year of MOBILE LTE (year 3). This analysis is referred to as the pooled analysis.

METHODS

Study design

- MOBILE LTE was a multinational, multicentre, partially randomised, double-blind extension study.
- Postmenopausal women who had completed 2 years of MOBILE and whose compliance with their monthly regimen was >75% were eligible – patients had to be ambulatory at the beginning of the trial and not expected to be hospitalised, immobilised or bedridden during the trial.
- Treatment was dependent on that received in MOBILE
 - patients previously treated with ibandronate 100mg monthly continued on 100mg monthly (group A)
 - patients previously treated with ibandronate 150mg monthly continued on 150mg monthly (group B)
 - patients previously treated with 2.5mg daily or 100mg over 2 consecutive days (50+50mg) were re-randomised to either group A or B
- To maintain blinding, patients also received a monthly placebo identical in appearance to the alternative dose.
- Patients included in the 3-year pooled analysis were those who received 100mg or 150mg monthly ibandronate for 2 years in the original MOBILE study and then remained on the same treatment during the first year of the LTE. Patient numbers in the third year of the pooled analysis were lower than years 1 and 2 as only 31 of the 65 centres from MOBILE participated in MOBILE LTE.
- Ibandronate was taken with plain water after an overnight fast (≥6 hours); patients were instructed to stay upright and fast for at least 1 hour after dosing.
- All patients also received daily oral calcium (500mg) and vitamin D (400IU) supplements.

Study endpoints

- For the pooled analysis, mean relative change from baseline (%) in lumbar spine, total hip, femoral neck and trochanter BMD were investigated – data are presented as mean relative change (%) from the original MOBILE baseline, providing a relative change in BMD for 3 years of continuous 100mg or 150mg ibandronate treatment.
- Changes in sCTX from baseline were also assessed.

Analysis populations

- The primary analysis population for all efficacy endpoints for the pooled analysis was the ITT population
 - data previously published from MOBILE 1 and 2 years are for the PP population and as such the data are not directly comparable.^{2,3}

RESULTS

Patient characteristics

- For the pooled analysis, 173 and 169 (168 for lumbar spine BMD) women continued treatment with 100mg and 150mg monthly oral dosing, respectively, and were followed up for BMD assessment for a third year.
- Patient characteristics for the overall MOBILE LTE population (ITT) were well balanced across the treatment arms (Table 1).

Table 1. Baseline patient demographics (ITT population; mean).

	Ibandronate 100mg monthly (n=347)	Ibandronate 150mg monthly (n=350)
Age (years)	67.6	67.6
Body mass index (kg/m ²)	25.9	26.0
Lumbar spine [L2-L4] BMD (g/cm ²)	0.79	0.80*
Lumbar spine [L2-L4] BMD (T-score)	-2.92	-2.90*
Total hip BMD (g/cm ²)	0.77	0.79*
sCTX (ng/mL)	0.20	0.18

*n=349
Baseline sCTX levels are the re-analysed results from the MOBILE 2-year samples (n=56 and 68 for 100mg and 150mg arms, respectively). Median values presented

Lumbar spine BMD

- The pooled analysis after the first year of the MOBILE LTE showed that lumbar spine BMD was consistently increased over 3 years of continuous treatment with monthly ibandronate (Figure 1)
 - at 3 years, a substantial increase of 7.6% was observed in the 150mg monthly arm (p<0.0001 vs baseline); notably, the additional increase in BMD from 2 to 3 years was highly significant (p<0.0001)
 - a 6.4% increase was observed in the 100mg monthly arm (p<0.0001 vs baseline); again, the additional increase in BMD from 2 to 3 years was significant (p=0.003).
- Analyses in the PP population confirmed these findings.

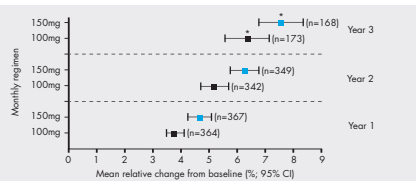


Figure 1. Mean relative change (%) from baseline in lumbar spine BMD with 3 years of continuous treatment with monthly ibandronate (ITT population; combined BMD analysis).

Proximal femur BMD

- Three years of continuous treatment with 150mg monthly ibandronate provided a significant total hip BMD increase of 4.1% versus baseline (p<0.0001; Figure 2)
 - in the 100mg monthly arm, total hip BMD was significantly increased by 3.4% (p<0.0001; Figure 2)
 - BMD increases over 3 years in the 100mg and 150mg arms were also significantly increased at the femoral neck (2.5% and 3.5%) and trochanter (5.4% and 6.2%), respectively (p<0.0001 vs baseline for all comparisons; Figures 3a and 3b).
- Analyses in the PP population confirmed these findings.

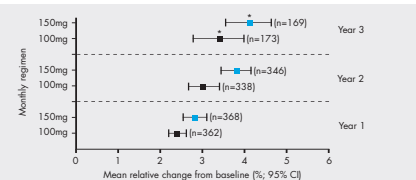


Figure 2. Mean relative change (%) from baseline in total hip BMD with 3 years of continuous treatment with monthly ibandronate (ITT population; combined BMD analysis).

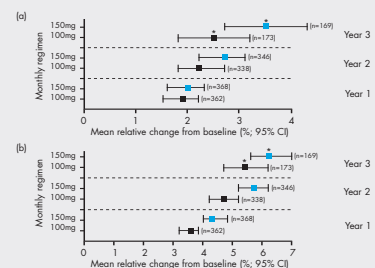


Figure 3. Mean relative change (%) from baseline in femoral neck (a) and trochanter (b) BMD with 3 years of continuous treatment with monthly ibandronate (ITT population; combined BMD analysis).

Changes in sCTX

- After the first year of MOBILE LTE (3 years of ibandronate treatment), sCTX concentrations remained within the premenopausal range. Relative to the MOBILE study baseline
 - median peak sCTX (month 30) decreased by 83.3% (150mg) and 70.1% (100mg; p<0.0001 for both)
 - median trough sCTX (month 36) decreased by 64.9% (150mg, p<0.0001) and 52.0% (100mg, p=0.0003).

Overall tolerability

- During the first year of MOBILE LTE, monthly ibandronate was well tolerated, with a generally comparable adverse event profile in the 100mg (n=359) and 150mg (n=360) treatment arms (Table 2).
- Importantly, the overall frequency of clinical osteoporotic fractures was low with a similar incidence across the two treatment arms (Table 2).

Table 2. Overall summary of adverse events at 1 year of MOBILE LTE (safety population; n[%]).

	Ibandronate 100mg monthly (n=359)	Ibandronate 150mg monthly (n=360)
Overall		
Any adverse event	201 (56.0)	192 (53.3)
Any drug-related adverse event	30 (8.4)	28 (7.8)
Any drug-related adverse event leading to withdrawal	1 (0.3)	3 (0.8)
Any drug-related serious adverse event	0	1 (0.3)
All upper GI disorders	16 (4.5)	25 (6.9)
Any upper GI adverse event leading to withdrawal	2 (0.6)	2 (0.6)
Clinical osteoporotic fracture	13 (3.6)	8 (2.2)

Drug-related adverse events include those with a causal relationship judged by the investigator to be probably, possibly or remotely related to study medication

Upper GI adverse events

- The incidence of upper GI adverse events and upper GI adverse events leading to withdrawal was comparable across the treatment arms (Table 2). No serious upper GI adverse events were reported.

CONCLUSIONS

- After the first year of MOBILE LTE, further increases in lumbar spine and total hip BMD were observed in patients receiving an additional year of 150mg monthly ibandronate.
- In the pooled analysis, lumbar spine and total hip BMD increased progressively in those patients who had received 3 years of continuous treatment with 150mg monthly ibandronate.
- Monthly oral ibandronate dosing was well tolerated with no disadvantage in the 150mg arm compared with the 100mg arm.
- These data show that 150mg monthly ibandronate provides consistent gains in BMD in postmenopausal women with osteoporosis. This, plus the favourable tolerability profile and greater persistence with monthly ibandronate versus weekly regimens⁵ support the clinical benefits.

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