

Rationale and design of the MOTION study (Monthly Oral Therapy with Ibandronate for Osteoporosis iNtervention)

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SUMMARY

- Active comparator studies are an accepted and necessary means for establishing the relative efficacy and safety of alternative treatment options; however, as clinical endpoints are often difficult to use (especially in chronic disease), comparison of validated surrogate markers is a valid alternative.
- In light of its predictive value for fracture risk reduction within the class of bisphosphonates, the surrogate marker of change (%) in bone mineral density (BMD) has recently been used to assess the relative efficacy of weekly oral bisphosphonates in postmenopausal osteoporosis.
- Specifically, versus weekly oral risedronate (35mg), weekly oral alendronate (70mg) was shown to provide significantly greater increases in BMD in the FACT study.
- A similar comparative study (MOTION) is currently ongoing to compare the efficacy and safety of the new once-monthly oral ibandronate (Boniva) regimen (150mg) with the efficacious weekly oral alendronate regimen (70mg) evaluated in FACT.
- In this multinational, randomized, double-blind, double-dummy, phase IIIb, non-inferiority study, approximately 1,800 women (aged 55–84 years, ≥5 years since menopause) with postmenopausal osteoporosis (lumbar spine [L2–L4] BMD T-score <−2.5 and ≥−5.0) are receiving 1 year's treatment with daily calcium (500–1,500mg) and vitamin D (400IU) plus either 150mg once-monthly ibandronate or 70mg weekly alendronate.
- The co-primary study endpoints are change (%) from baseline in total hip and lumbar spine BMD at 1 year.
- To establish therapeutic equivalence, increases in the once-monthly and weekly treatment arms at both sites will then be compared by non-inferiority test.
- Secondary endpoints include: change (%) from baseline in hip trochanter BMD at 1 year and serum CTX and P1NP at day 7, months 3 and 6, day 7 after month 6, and month 12.
- Adverse events, including clinical fractures, will be monitored throughout the study.
- In summary, MOTION will explore the relative efficacy and safety of once-monthly oral ibandronate versus the efficacious weekly oral alendronate regimen.
- Study outcomes will further assist physicians in identifying the most appropriate treatment option in postmenopausal osteoporosis.

INTRODUCTION

- When effective therapies are available, active comparator studies are indicated to assess the relative efficacy of alternative treatment options.
- In chronic disease, comparison of validated surrogate markers may be indicated, as clinical endpoints are often difficult to assess.

- In osteoporosis, the surrogate marker of change (%) in BMD has recently been used to establish the relative efficacy of weekly oral bisphosphonates in postmenopausal osteoporosis, given its predictive value for fracture risk reduction within the bisphosphonate class.¹
- Specifically, when compared with those receiving weekly oral risedronate (35mg), patients receiving

weekly oral alendronate (70mg) obtained significantly greater increases in proximal femur (all sites) and lumbar spine BMD in the FACT study.¹

- A similar comparative study (MOTION) is ongoing to establish the relative efficacy of the new once-monthly oral ibandronate dosing regimen with the efficacious weekly oral alendronate regimen evaluated in FACT.
- Here, we summarize the design and conduct of the MOTION study.

METHODS

Study design and participants

- Ongoing, multinational, randomized, double-dummy, phase IIIb, non-inferiority study.
- A total of 90 centers in North America, Latin America, Europe and South Africa.
- Approximately 1,800 women (aged 55–84 years; ≥5 years postmenopause) with postmenopausal osteoporosis (mean lumbar spine [L2–L4] BMD T-score <−2.5 and ≥−5.0).
- All participants randomly assigned to either once-monthly oral ibandronate (150mg) or weekly oral alendronate (70mg) for 1 year (plus 15 additional days of follow-up) (**Figure 1**).
- All patients receiving once-monthly or weekly oral placebo medication to maintain blinding.
- Daily calcium (500–1,500mg) and vitamin D (400IU) supplements also provided (**Figure 1**).

Study endpoints

- Co-primary efficacy endpoints: mean change (%) from baseline in total hip and lumbar spine BMD at 1 year.
- Secondary efficacy endpoints
 - mean change (%) from baseline in hip trochanter BMD at 1 year

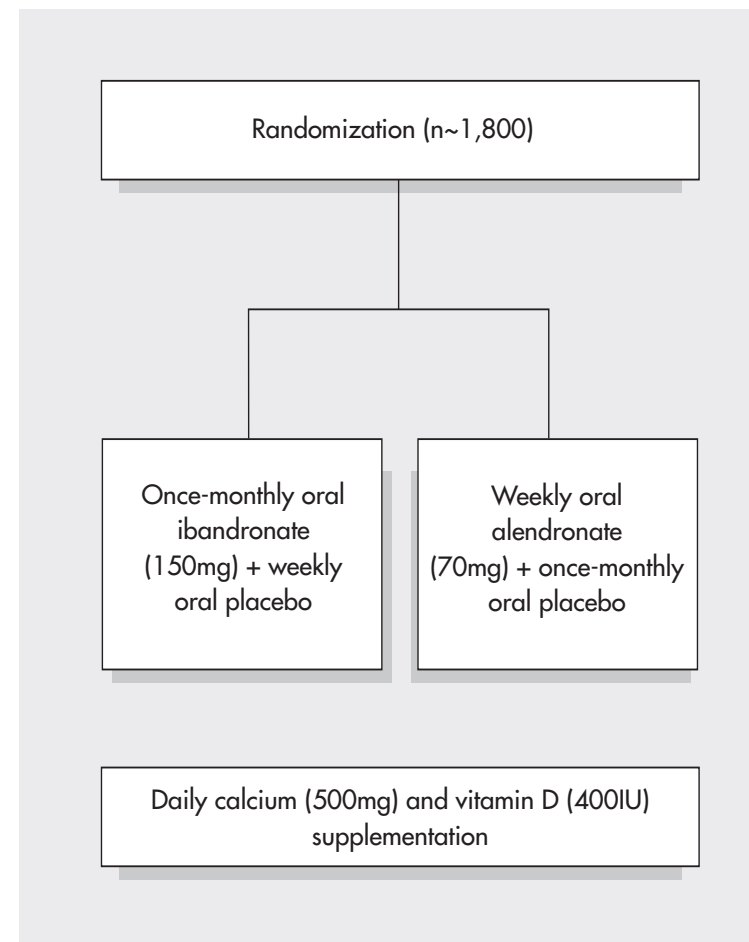


Figure 1. Design of the MOTION study.

- median change (%) from baseline in serum CTX and P1NP at day 7, months 3 and 6, day 7 after month 6, and month 12 (in approximately 30% of the study population)
- proportion (%) of participants with mean increases in total hip and/or lumbar spine BMD above baseline and 3% and 6%, respectively (exploratory analysis).
- Safety parameters: adverse events, including clinical vertebral and non-vertebral fractures, are monitored throughout the study; safety laboratory parameters are also assessed.

Statistical analysis

- Changes (%) in total hip and lumbar spine BMD with the once-monthly and weekly regimens will be compared by non-inferiority test at 1 year.
- In a prior study, the minimum difference between weekly alendronate and placebo at 1 year was 2.9% at the total hip and 4.7% at the lumbar spine (in MOTION, the monthly regimen is assumed to have the same effect as the daily regimen).²
- Non-inferiority margins are set at 30% of these differences (0.87% and 1.14%, respectively), thereby preserving at least 70% of the effect of the weekly regimen.
- On this basis, non-inferiority will be concluded if the lower boundary of the one-sided 97.5% confidence intervals for the between-group difference in the mean change in total hip BMD is ≥−0.87% and lumbar spine BMD is ≥−1.14%.

CONCLUSIONS

- MOTION will explore the relative efficacy and safety of once-monthly oral ibandronate (150mg) versus the efficacious weekly oral alendronate regimen (70mg) evaluated in FACT.
- Study outcomes will further assist physicians in identifying the most efficacious, well tolerated and patient-friendly treatment option in postmenopausal osteoporosis.

REFERENCES

1. Rosen C, et al. J Bone Miner Res 2005;20:141–51.
2. Hosking D, et al. Curr Med Res Opin 2003;5:383–94.