



Alendronate* 70 mg Once Weekly and Alendronate 10 mg Once Daily Preference Study in Postmenopausal Women with Osteoporosis

*Trademark: Fosamax®, Merck & Co., Inc., West Point, PA

E.M. Lewiecki, MD¹, C. Rosen, MD², R.S. Bockman, MD, PhD³, L.K. Vanaman, RN⁴, L. Wang, PhD⁴, J. Yates, MD⁴, J. Palmisano, MD⁴, M.E. Smith⁴.

¹New Mexico Clinical Research & Osteoporosis Center, Albuquerque, NM, ²Maine Center for Osteoporosis, Bangor, ME, ³Hospital for Special Surgery, New York, NY, ⁴Merck & Co., Inc., West Point, PA.

Introduction

Osteoporosis is a major public health threat for more than 28 million Americans. Osteoporosis is responsible for more than 1.5 million fractures annually at an estimated cost of \$13.8 billion in 1995.¹

The recent availability of once weekly alendronate (Fosamax®) 70 mg provides an additional treatment option to once daily alendronate (Fosamax®) 10 mg. In an earlier study, both alendronate 70 mg once weekly and alendronate 10 mg once daily were well tolerated with a similar incidence of upper GI adverse experiences.²

Preference, convenience, and overall compliance are key factors in the successful treatment of chronic disease and thus the rationale for this study.

Results are reported for this randomized, open-label, cross-over designed clinical study which assessed patient preference, convenience, and overall compliance with once weekly alendronate and with once daily alendronate. Subject outcomes were determined by questionnaire given to post-menopausal women with osteoporosis.

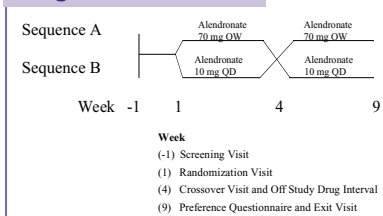
¹ National Osteoporosis Foundation

² Schnitzer T, Bone HG, Crepaldi G, et al. Therapeutic equivalence of alendronate 70 once-weekly and alendronate 10 mg daily in the treatment of osteoporosis. *Aging Clin. Exp. Res.* 12:1-12, 2000.

Entry Criteria

- Postmenopausal women with osteoporosis
- Naive to all therapies for the treatment of osteoporosis including:
 - bisphosphonates, calcitonin, and SERMS
- Generally in good health

Design Overview



Methodology

- Assuming 61% of patients prefer alendronate 70 mg once weekly, a total of 240 patients (120 patients per treatment sequence) will provide 93% power to distinguish alendronate 70 mg once weekly preference from the null hypothesis of no preference
- Gart's Test at the 5% level of significance

Study Design

- 9-week, open-label, randomized crossover
- 279 women randomized at 40 U.S. sites
- Randomized 1:1 ratio:

Treatment Sequence (Alendronate)	Period 1 Week 1-Week 4	Off Therapy Week 5	Period 2 Week 6-Week 9
Sequence A	70 mg once weekly	No alendronate	10 mg once daily
Sequence B	10 mg once daily	No alendronate	70 mg once weekly

- Questionnaire completed by patient to determine which treatment regimen alendronate once weekly or alendronate once daily:
 - Is preferred
 - Is considered the most convenient
 - Would provide greater overall long term compliance

Baseline Characteristics

	Sequence A ALN Once Weekly to ALN Once Daily n=142	Sequence B ALN Once Daily to ALN Once Weekly n=145
Caucasian Women (%)	93.7	89.0
Age (mean years ± SD)	64.0 ± 9.3	65.6 ± 9.89
Age at menopause (mean years ± SD)	46.2 ± 7.8	45.9 ± 7.9
Caffeine intake > 3 cups/day (%)	24.5	16.6
Smoking:		
Current (%)	16.1	15.2
Previous (%)	24.5	31.7

Patient Disposition

	Sequence A ALN Weekly 70 mg to ALN Daily 10 mg N=143 n=(%)	Sequence B ALN Daily 10 mg to ALN Weekly 70 mg N=145 n=(%)	Total N=287 n=(%)
Completed Study	133 (93.0)	133 (91.7)	266 (92.4)
Discontinued	10 (7.0)	12 (8.3)	22 (7.6)
Reasons for Discontinuation:			
Clinical AE	9 (6.3)	8 (5.5)	17 (5.9)
Lost to Follow-up	0 (0)	2 (1.4)	2 (0.7)
Withdrew Consent	1 (0.7)*	1 (0.7)	2 (0.7)
Other	0(0.0)	1 (0.7)	1 (0.3)

*Patient never treated

Most Frequently Reported AEs

(Incidence ≥ 2% in either treatment group)

Adverse Experience	Alendronate Once Weekly 70 mg N=277 (%)	Alendronate Once Daily 10 mg N=283 (%)
Diarrhea	11 (4.0)	7 (2.5)
Nausea	10 (3.6)	6 (2.1)
Constipation	4 (1.4)	8 (2.8)
Headache	3 (1.1)	8 (2.8)

*No significant differences between treatment groups

RESULTS SUMMARY

Preference Question:

- 86.4% (235/272) Preferred alendronate once-weekly regimen
- 9.2% (25/272) Preferred alendronate once-daily regimen
- 4.4% (12) had no preference

Convenience Question:

- 89.0% (242/272) considered alendronate once-weekly regimen to be more convenient
- 7.7% (21/272) considered alendronate once-daily regimen to be more convenient
- 3.3% (9) considered alendronate once-weekly and alendronate once-daily regimen to be equally convenient

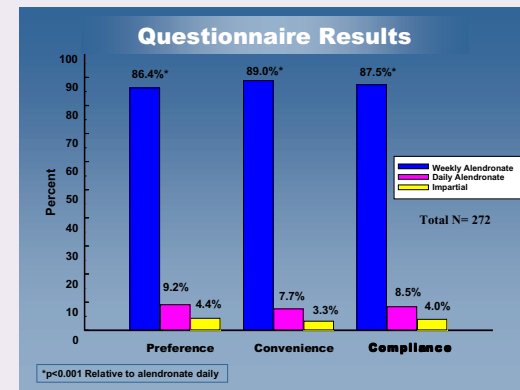
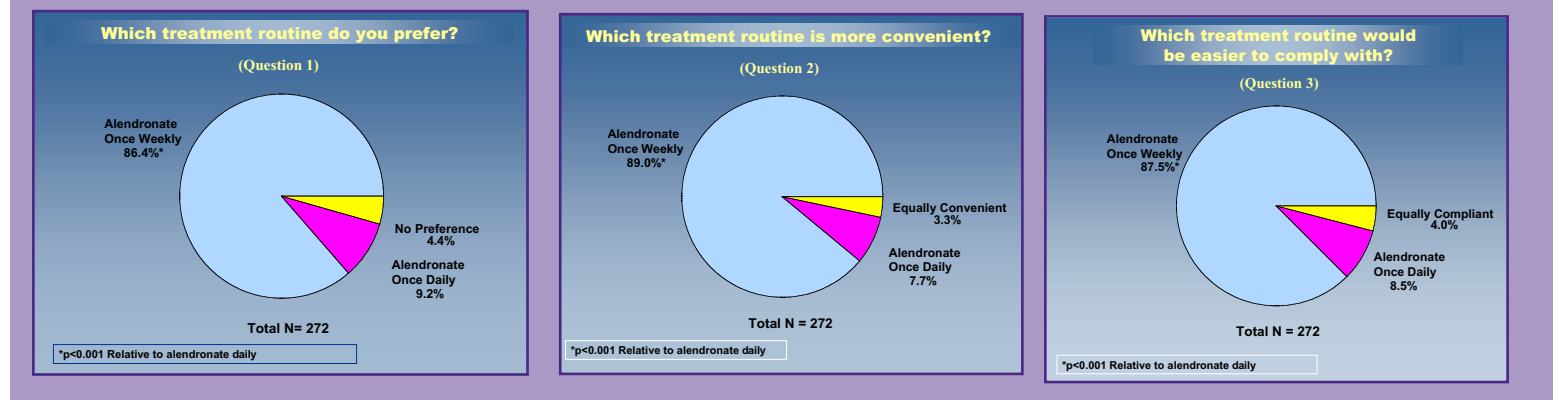
Compliance Question:

- 87.5% (238/272) considered alendronate once-weekly regimen easier to comply
- 8.5% (23/272) considered alendronate once-daily regimen easier to comply
- 4.4% (12) considered both alendronate once-daily and alendronate once-daily regimens equally easy to comply

CONCLUSIONS

- When alendronate 70 mg administered once weekly is compared to alendronate 10 mg administered once daily:
 - alendronate 70 mg once weekly is the preferred dosing regimen as measured by a questionnaire
 - alendronate 70 mg once weekly is considered more convenient
 - alendronate 70 mg once weekly provides greater overall long term compliance
- In this open-label crossover study, both alendronate 70 mg administered once weekly and alendronate 10 mg once daily were safe and well tolerated and had a similar incidence of adverse events.

QUESTIONNAIRE RESULTS



QUESTIONNAIRE

You have just completed this study and have followed two different osteoporosis treatment routines: you have taken the osteoporosis medication once a week and you have taken it once a day. It is important to remember that the osteoporosis medications you took during these two treatment routines have the same beneficial effect for your bones in terms of bone density. Please answer the three questions below. We encourage you to choose the answer that best describes your experience.

For each question, please check **one** box only

1. Which treatment routine do you prefer?

- I prefer the once a week treatment routine
- I prefer the once a day treatment routine
- I do not prefer one treatment routine over the other treatment routine

2. Which treatment routine is more convenient?

- The once a week treatment routine is more convenient
- The once a day treatment routine is more convenient
- The once a week treatment routine and the once a day treatment routine are equally convenient

3. The word "comply" means to follow a treatment routine as instructed by your doctor. Which treatment routine would be easier to comply with for a long period of time?

- It would be easier to comply with the once a week treatment routine for a long period of time
- It would be easier to comply with the once a day treatment routine for a long period of time
- It would be equally easy to comply with the once a week treatment routine and the once a day treatment routine for a long period of time