

# Patient Preference of Once Weekly or Daily Administration of Alendronate (Fosamax) for Osteoporosis: A Randomized Cross-Over Study

Kendler DL,<sup>1</sup> Diez-Perez A,<sup>2</sup> Gaines KA,<sup>3</sup> Verbruggen N,<sup>3</sup> and Melton ME<sup>3</sup>

<sup>1</sup>St. Vincent's Hospital, Vancouver, British Columbia, Canada, <sup>2</sup>Hospital del Mar, Barcelona, Spain, <sup>3</sup>Merck & Co., Inc., Whitehouse Station, NJ, USA

## Background

It is well accepted that patients prefer a daily dosing regimen to dosing several times a day. Whether patients would prefer even less frequent dosing, such as once weekly dosing, is unknown.

Alendronate dosed once weekly has now been shown to have equivalent efficacy to once daily dosing [Schnitzer, *et al.*, Aging Clin Exp Res 12:1-12, 2000]. This study was designed to examine preference for a once weekly or a once daily alendronate dosing regimen in postmenopausal women initiating treatment for osteoporosis. A similar study conducted in the US demonstrated a strong preference for the once weekly regimen (90% of patients preferred the once weekly to the daily regimen) (Lewiecki, *et al.*, ASBMR 2001).

## Purpose of the Study

To determine which regimen, alendronate 70 mg administered once weekly or alendronate 10 mg administered daily, is **preferred** by postmenopausal women with osteoporosis. In addition, to assess patient response to parameters of **convenience** and **willingness to take long term**.

## Study Design

- 9-week, open-label, randomized crossover study
- 45 participating centers in 19 countries representative of Europe, the Americas, and the Asia Pacific region
- 406 postmenopausal women with osteoporosis were randomized
- Randomized 1:1 ratio to alendronate (ALN) 70 mg once weekly (OW) followed by 10 mg daily (D), or vice versa:

Treatment Sequence (ALN)	Period 1 Week 1-Week 4	Off Therapy Week 5	Period 2 Week 6-Week 9
Sequence A	70 mg OW	No ALN	10 mg D
Sequence B	10 mg D	No ALN	70 mg OW

- Patients completed a dosing regimen questionnaire after experiencing each dosing regimen

## Entry Criteria

- Postmenopausal women with osteoporosis
- Naïve to all therapies for the treatment of osteoporosis including bisphosphonates, calcitonin, and SERMS
- HRT, calcium, vitamin D allowed
- Generally in good health

## Endpoints

- Primary**
  - Preference of patients for a dosing regimen
- Secondary**
  - Assessment of convenience
  - Willingness to take long-term
  - Safety and tolerability

## Methods

- The analysis included all patients who took at least one dose of each regimen and expressed a preference
- The percentage of patients preferring alendronate 70 mg once weekly was evaluated using Mainland-Gart's test for a binomial response in a two-treatment, two-period crossover study
- Subgroup analyses were conducted to examine any association of country of residence, age, concomitant medications and chronic disease on regimen preference

## Dosing Regimen Questionnaire

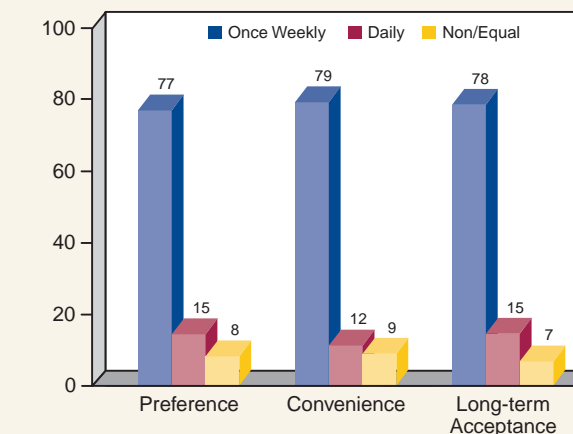
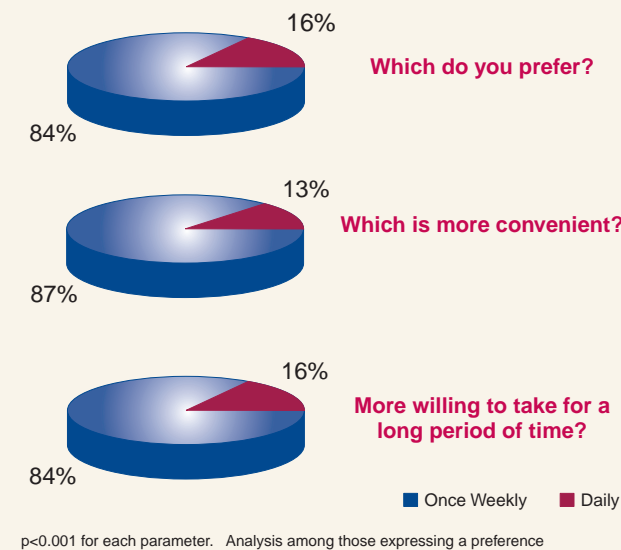
For each question, please check **one** box only

- Which treatment routine do you prefer?**
  - I prefer the once a week treatment routine
  - I prefer the once a day treatment routine
  - I have no preference
- 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
- Which treatment would you be more willing to take for a long period of time?**
  - I would be more willing to take the once a week treatment for a long period of time
  - I would be more willing to take the once a day treatment for a long period of time
  - I would be equally willing to take either the once a week or the once a day treatment for a long period of time

## Baseline Characteristics

	Sequence A OW-D N=201	Sequence B D-OW N=205	Total N=406
Age (Yrs)	63.1	63.0	63.0
Race			
Caucasian	64 %	66 %	65 %
Asian	23 %	20 %	22 %
Hispanic	8 %	8 %	8 %
Other	5 %	6 %	5 %
BMI (kg/m <sup>2</sup> )	25.0	25.3	25.2
Yrs since last menses	16.4	16.8	16.6
Family history of osteoporosis	39 %	38 %	39 %

## Results



p<0.001 comparison of alendronate once weekly to alendronate daily. Analysis of all responses.

## Subgroup Analyses of Patient Preference

	Total with Preference	Preference for Alendronate 70 mg Once Weekly	
	N	N	(%) 95% CI <sup>†</sup>
<b>Age (p=0.113)</b>			
≤ 65 year	232	189	(81.5%) (75.9, 86.2)
> 65 year	132	116	(87.9%) (81.1, 92.9)
<b>More than 75% of time with concomitant medication (p=0.981)</b>			
No	49	41	(83.7%) (70.3, 92.7)
Yes	315	264	(83.8%) (79.3, 87.7)
<b>Number of active medical conditions (p=0.872)</b>			
0	73	67	(91.8%) (83.0, 96.9)
1	75	59	(78.7%) (67.7, 87.3)
2	59	47	(79.7%) (67.2, 89.0)
3	40	34	(85.0%) (70.2, 94.3)
4	38	28	(73.7%) (56.9, 86.6)
5	18	17	(94.4%) (72.7, 99.9)
6 - 10	45	39	(86.7%) (73.2, 94.9)
11 - 15	9	8	(88.9%) (51.8, 99.7)
>15	7	6	(85.7%) (42.1, 99.6)
<b>Number of concomitant chronic medication (p=0.215)</b>			
None	49	41	(83.7%) (70.3, 92.7)
At least one	315	264	(83.8%) (79.3, 87.7)

<sup>†</sup>95% Confidence interval based on binomial distribution. Results consistent across countries. No sequence effect seen.

## Overall Adverse Experience Summary

Number of Patients	ALN 70 mg OW (N=403)		ALN 10 mg OD (N=399)	
	N	(%)	N	(%)
With one or more adverse experiences	99	(24.6)	110	(27.6)
With a drug-related adverse experience <sup>†</sup>	30	(7.4)	40	(10.0)
With a serious adverse experience	4	(1.0)	5	(1.3)
Who discontinued for an adverse experience	6	(1.5)	9	(2.3)

Although a patient may have had two or more adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

<sup>†</sup>Considered possibly, probably or definitely drug-related by the investigator.

## Conclusions

Alendronate dosed once weekly, when compared to alendronate dosed daily, is preferred by the overwhelming majority (84%) of patients. In addition, the once weekly regimen is considered by most patients to be more convenient and is the regimen they are more willing to take long term. Preference for once weekly dosing was similar across all subgroups analyzed. This strong preference for the once weekly alendronate regimen is similar to and confirms the results from a study conducted in the US in which 90% of patients preferred once weekly, 92% found it more convenient, and 91% were more likely to comply with it. (Lewiecki *et al.*, ASBMR 2001).

These studies now establish that postmenopausal women with osteoporosis have an overwhelming preference for the alendronate once weekly regimen.