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Patient Satisfaction in Postmenopausal Women Treated with a Weekly Bisphosphonate Transitioned to Once-Monthly Ibandronate

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Abstract

Objective: CURRENT, a large, open-label, 6-month, multicenter study, was designed to assess patient satisfaction levels and patient treatment preference after switching from weekly oral bisphosphonates to monthly oral ibandronate for a period of 6 months.

Methods: This study enrolled postmenopausal women who had taken a weekly oral bisphosphonate for at least 3 months for prevention or treatment of osteoporosis or osteopenia at the time of screening. Enrolled patients were switched to 150 mg monthly ibandronate. At baseline and 6 months, patients completed the Osteoporosis Patient Satisfaction Questionnaire (OPSAT-QTM), consisting of four domains. Scores were converted to composite satisfaction scores (scale of 0–100). At 6 months, patients completed the Preference Questionnaire. Adverse events were monitored throughout.

Results: The intent-to-treat population comprised 1678 patients. OPSAT-Q composite satisfaction scores improved by 9 points by month 6 despite the high mean baseline summary scores (80.1 points). Convenience, overall satisfaction, and quality of life domain scores improved by 15.6, 12, and 9.2 points, respectively. Increased satisfaction was reported by the majority of patients at month 6 (70.4%). Patients who reported stomach upset or suboptimal compliance with prestudy weekly bisphosphonate treatment were more likely to report improved satisfaction (odds ratio [OR] for stomach upset 2.98, 95% CI 1.52, 6.50, $p = 0.0026$; suboptimal compliance 1.82, 95% CI 1.13–3.04, $p = 0.017$). After 6 months, 73.6% of patients preferred monthly ibandronate to weekly bisphosphonates. The most frequently occurring adverse events were upper respiratory tract infection (3.2% of patients), dyspepsia (2.5%), fracture (2.4%), arthralgia (2.3%), and gastroesophageal reflux disease, diarrhea, and nausea (2.2% each).

Conclusions: Patients previously using weekly bisphosphonates reported improved satisfaction with monthly ibandronate dosing.

Introduction

BISPHOSPHONATES ARE THE PREFERRED medication treatment option for the management of postmenopausal osteoporosis.¹ Although the efficacy of bisphosphonates in increasing bone mineral density and reducing the risk of fractures in patients with osteoporosis has been demonstrated

in clinical trials, their effectiveness in real-life clinical settings is often compromised by poor compliance and persistence.^{2–4}

The reasons for poor compliance and persistence with oral bisphosphonates reflect a number of issues, including the lack of symptoms of osteoporosis (until a fracture occurs), the lengthy time taken before the benefits of treatment are seen, the stringent dose administration requirements specified, and

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patients' concern over possible side effects. Patients' desire to continue therapy has been shown to be related to satisfaction with treatment for diseases other than osteoporosis.^{5,6} Evidence suggests that compliance with treatment is linked to fracture risk in postmenopausal women with osteoporosis.^{2,7} Thus, better compliance might be expected to improve clinical outcomes. One approach to improving compliance with oral bisphosphonates has been lengthening the dosing intervals from daily to weekly and, most recently, to monthly. Quarterly and yearly intravenous dosing regimens have also been developed.

The objective of the CURRENT study was to identify the level of patient satisfaction with monthly bisphosphonate therapy in patients previously treated with weekly bisphosphonates, using the Osteoporosis Patient Satisfaction Questionnaire (OPSAT-Q)TM. An additional objective of the study was to assess patients' treatment preferences after 6 months of treatment with monthly oral ibandronate.

Patients and Methods

Study design

CURRENT was a large, prospective, open-label, multicenter, 6-month study. The protocol, any modifications, and appropriate consent procedures were reviewed and approved by each study site's institutional review board. Written informed consent was obtained from each patient prior to participation in the study.

Patients

Inclusion criteria. Ambulatory postmenopausal women were eligible for inclusion in the study if they had been receiving weekly alendronate or risedronate for the prevention or treatment of osteoporosis or osteopenia for a minimum of 3 months, were able to understand the questionnaires, were willing to comply with the protocol, were able to understand and sign the written informed consent, and completed the screening questionnaire. The screening questionnaire consisted of three questions to which a Yes response indicated (1) a preference for monthly dosing over weekly, (2) experience of stomach upset within 48 hours of taking previous osteoporosis medication more than once a month, and (3) missing three or more doses of previous weekly osteoporosis medication in the last 3 months, respectively.

Exclusion criteria. Patients were excluded from the study if they had a hypersensitivity to bisphosphonates, had contraindications to calcium or vitamin D therapy, had received any investigational drug within 30 days, were unable to stand/sit in an upright position for at least 60 minutes, or were unable to swallow a tablet whole. A history of malignant disease within the previous 10 years (except resected basal cell cancer) or a history of liver disease, renal disease, or hypercalcemia was exclusionary. In addition, patients were excluded if they had a major upper gastrointestinal disease, such as significant upper gastrointestinal bleeding, within the last year requiring hospitalization or transfusion, recurrent peptic ulcer disease documented by radiographic or endoscopic means, ongoing dyspepsia or gastroesophageal reflux uncontrolled by medication, ongoing esophageal abnormalities that delay esophageal emptying (e.g., stricture, achalasia, or dysmotility), or active gastric/duodenal ulcers.

Patients were also excluded if the results of specified laboratory tests were abnormal: alanine aminotransferase (ALT) levels greater than twice the upper limit of the normal range, calcium >10.5 mg/dL or <8.0 mg/dL (>2.6 or <2.0 mmol/L), white blood cell count <2500/ μ L, serum albumin <3.0 g/L, or serum creatinine >2.4 mg/dL (>210 μ mol/L).

Study drug administration

Participants discontinued their current bisphosphonate treatment for a minimum of 1 week before starting 150 mg monthly oral ibandronate. Patients took one 150 mg tablet of ibandronate monthly for a period of 6 months for a total of six planned doses. Patients were instructed to fast overnight for at least 6 hours and to swallow their tablet whole with a full glass of plain water while sitting or standing in an upright position. They were to remain upright for 1 hour after dosing and to wait at least 1 hour before consuming any food or beverage other than water. Patients were instructed not to take supplemental calcium or vitamin D or any other drug during the postdose fasting period. Patients could elect to receive a monthly reminder to take their medication. Compliance was assessed by recording drug dispensed and returned. Patients were also instructed to take supplemental calcium and vitamin D for the full duration of the study, which was taken in divided daily doses with meals.

Treatment satisfaction and preference assessments

The OPSAT-Q was completed at baseline and at the end of the study. The OPSAT-Q (Table 1) is a validated questionnaire designed to capture satisfaction with bisphosphonate treatment. It comprises four domains: convenience (questions 1–6), quality of life (questions 7 and 8), overall satisfaction (questions 9 and 10), and side effects (questions 11–16).⁸ All items were scored such that higher scores represented greater satisfaction or less bother/frequency of side effects. Treatment satisfaction was measured with the OPSAT-Q composite satisfaction score (OPSAT-Q CSS), which was the average of the scores from the four domains of the OPSAT-Q converted to a 0–100-point scale. In a psychometric evaluation, the individual items of the OPSAT-Q were found to be significantly correlated with the domain scores and CSS, and the domain scores and OPSAT-Q CSS were found to be internally consistent (Cronbach's alpha for domains ranged from 0.72 to 0.89 and was 0.87 for the CSS).⁸ Significant correlations were identified between OPSAT-Q scores and global demographic measures and quality of life scales, supporting the construct validity of the OPSAT-Q.⁸

Patients also completed the Preference Questionnaire (Pref-Q) (Table 2) at study end or on withdrawal. The Pref-Q was adapted from a questionnaire used in an earlier study of daily and weekly formulations of another bisphosphonate and validated by the MEDTAP Institute Inc. (Bethesda, MD).⁹

Safety assessments

Patients attended monthly clinic visits during the study. Adverse events (AEs) were monitored and recorded at visits and through phone calls from patients throughout the study. Patients were followed for 15 days after completion of treatment to record any AEs. The results of laboratory tests at screening and final visit were reviewed by the investigator for

TABLE 1. OSTEOPOROSIS PATIENT SATISFACTION QUESTIONNAIRE (OPSAT-Q™)

This questionnaire asks about how satisfied or dissatisfied you are with the medication you have been taking for osteoporosis or osteopenia. Please answer each question by marking an X in the box that most closely represents the way you feel. There are no right or wrong answers.

Please indicate how satisfied or dissatisfied you are with the following

	Very dissatisfied	Dissatisfied	Somewhat dissatisfied	Neither satisfied nor dissatisfied	Somewhat satisfied	Satisfied	Very satisfied
1. How well the medication fits into your overall medication schedule	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. How often you have to take the medication	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. The convenience of taking the medication	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. How easy it is to take the medication	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. How easy it is to remember to take the medication	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. The amount of time required to take the medication, including staying upright	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. How well the medication gives you confidence to participate in your daily home and/or work activities	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. How well the medication gives you confidence to be as physically active as you'd like to be	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Overall, how satisfied are you with your medication?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. How satisfied would you be to continue taking the medication?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

How bothered are you by the following side effects that you may or may not experience after taking your osteoporosis/osteopenia medication? If you have never experienced the side effect from the medication, please answer Not at all bothered.

	Not at All bothered	Slightly bothered	Moderately bothered	Quite a bit bothered	Extremely bothered
11. Heartburn or acid reflux	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. Stomach upset other than heartburn or acid reflux (such as diarrhea, nausea, vomiting, or stomach pain)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Any other side effects you think are related to your osteoporosis medication	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

During the past 4 weeks, on approximately how many days did you experience the following side effects associated with your osteoporosis/osteopenia medication?

	0 Days	1 Day	2 Days	3 Days	More than 3 days
14. Heartburn or acid reflux	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15. Stomach upset other than heartburn or acid reflux (such as diarrhea, nausea, vomiting, or stomach pain)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16. Any other side effects you think are related to your osteoporosis medication	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Thank you for completing this questionnaire!

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any abnormal findings. Laboratory abnormalities were not reported as AEs unless they caused a clinically relevant condition (i.e., were clinically meaningful).

Statistical analyses

All statistical analyses were predetermined and specified in the study protocol. The populations used to analyze the study end points were as follows: (1) the intent-to-treat (ITT) population, comprising all participants who received at least one

dose of study medication, (2) the safety analysis population, comprising all patients who received at least one dose of study medication and had at least one postbaseline safety measurement that gave evidence of contact with a study investigator (such as any AE report, laboratory measurement, physical examination, vital sign measurement, or other data); and (3) the *per-protocol* population, comprising ITT participants without significant protocol violations. Patients with missing responses to questions on the OPSAT-Q were excluded from the analysis for that domain of the OPSAT-Q.

TABLE 2. PREFERENCE QUESTIONNAIRE

INSTRUCTIONS: You have taken osteoporosis medication once a month and once a week. This questionnaire asks about what you think of these two treatment schedules. Please answer the questions by checking the appropriate boxes.

1. Which dosing schedule do you prefer? (*check one box only*)
 - I prefer the once-monthly dosing schedule. Go to Question 2.
 - I prefer the once-weekly dosing schedule. Go to Question 3.
 - I do not prefer one dosing schedule over the other dosing schedule. Go to Question 4.
2. If you prefer the once-monthly dosing schedule, please check all the statements you agree with. (*check all that apply*)
 - The once-monthly dosing schedule causes less stomach discomfort.
 - It is easier to tolerate side effects overall with the once-monthly dosing schedule.
 - The once-monthly dosing schedule fits better into my lifestyle.
 - It would be easier to follow the once-monthly dosing schedule for a long period of time.
 - I do not agree with any of the above. Go to Question 4.
3. If you prefer the once-weekly dosing schedule, please check *all* the statements you agree with. (*check all that apply*)
 - The once-weekly dosing schedule causes less stomach discomfort.
 - It is easier to tolerate side effects overall with the once-weekly dosing schedule.
 - The once-weekly dosing schedule fits better into my lifestyle.
 - It would be easier to follow the once-weekly dosing schedule for a long period of time.
 - I do not agree with any of the above. Go to Question 4.
4. Which dosing schedule is more convenient? (*check one box only*)
 - The once-monthly dosing schedule is more convenient.
 - The once-weekly dosing schedule is more convenient.
 - The once-monthly dosing schedule and the once-weekly dosing schedule are equally convenient.

Thank you for completing this questionnaire!

The significance of the absolute change in scores from baseline to month 6 for both the OPSAT-Q CSS and the individual domain scores was calculated using a *t* test or non-parametric test, as appropriate. Satisfaction rates were examined using a range of definitions for satisfaction responders: patients with OPSAT-Q CSS increases of 5% or more, 10% or more, 5 points or more, or 10 points or more from baseline to month 6, and the number of patients with an

OPSAT-Q CSS of >80 points at 6 months. Demographic characteristics and responses on the screening questionnaire were correlated with increase in the CSS using a logistic regression model.

Patient preference is presented as the percentage of patients who expressed a preference for monthly treatment, weekly treatment, or neither. The number and proportion of patients who had $\geq 80\%$ compliance with 6 monthly doses of iban-

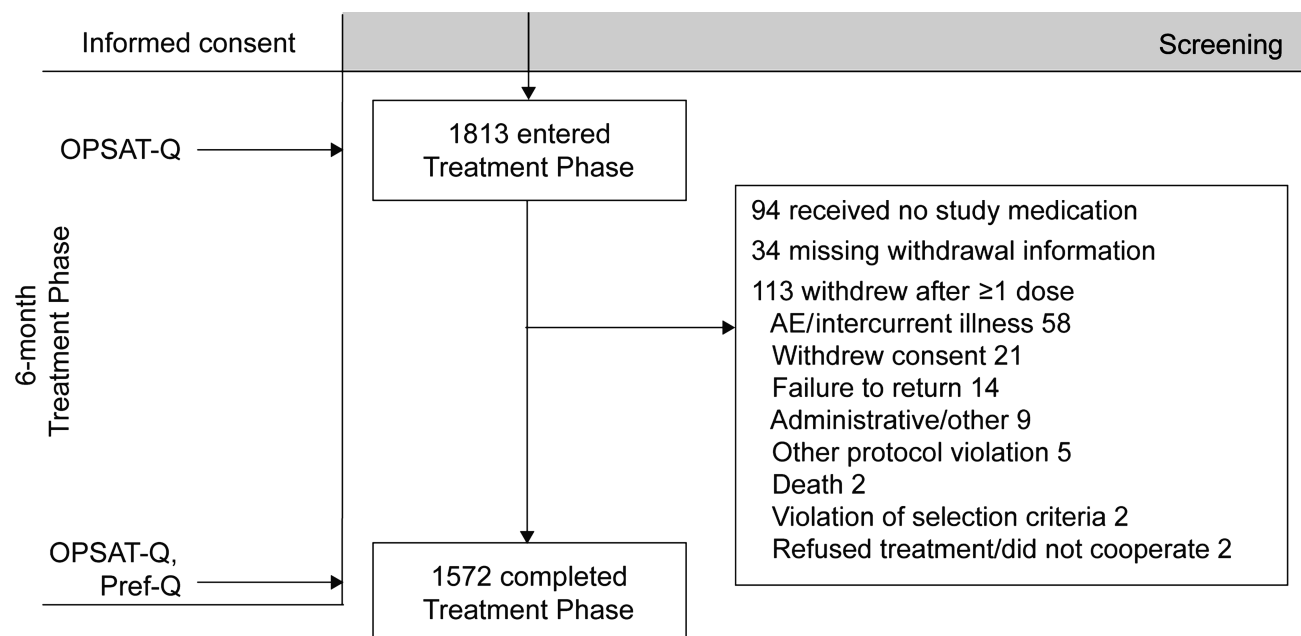


FIG. 1. Study design and patient disposition.

dronate and patients who requested a monthly reminder were summarized using descriptive statistics.

Results

Study population

One hundred forty-four clinical sites in the United States participated in this study. The disposition of patients in the study is summarized in Figure 1. Of the 1813 patients who entered the treatment phase, 1572, or 86.7%, completed treatment. The ITT population included 1678 patients who received at least one dose of study medication. The safety population included the 1669 ITT patients who had at least one safety measurement after their first dose of ibandronate. The *per-protocol* population consisted of 1319 patients after exclusion of 359 ITT patients (191 took excluded concomitant medications, 101 did not take at least five doses of study medication, 43 had no baseline or final OPSAT-Q CSS, 51 had not received at least 3 months of weekly alendronate or risendronate before entering the study, and 24 did not meet other study entry criteria; some patients were excluded for multiple reasons). The baseline demographic and clinical characteristics of the 1678 patients in the ITT population are presented in Table 3.

During the study, 6.7% of patients withdrew after taking one or more doses of study medication. The most common reasons for withdrawal were AEs/intercurrent illness (3.5%, discussed in the *Safety* section) and consent withdrawn (1.3%).

Changes in satisfaction

Although mean OPSAT-Q CSS and OPSAT-Q domain scores were high at baseline for weekly bisphosphonate use, statistically significant improvement was observed in mean OPSAT-Q CSS and in the convenience, quality of life, and overall satisfaction OPSAT-Q domain scores after 6 months of monthly ibandronate treatment (Table 4). The side effects OPSAT-Q domain score remained at approximately baseline levels. The proportion of patients who showed improvement in satisfaction compared with baseline after 6 months was 70.4% (1087 of 1543). The proportions of patients classified as satisfaction responders according to the prespecified definitions are summarized in Figure 2. The results for the *per-protocol* population were similar to the results in the ITT population (data not shown).

The proportions of patients with higher OPSAT-Q CSSs compared with baseline after 6 months' treatment with monthly ibandronate, stratified by demographic and baseline characteristics, are shown in Figure 3.

Using a logistic regression model, age, stomach upset within 48 hours of taking their previous weekly bisphosphonate more than once a month, and missing three or more doses of their previous weekly bisphosphonate in the past 3 months were significantly correlated with increase in OPSAT-Q CSS at month 6 compared with baseline. Patients <65 years of age were 1.7 times more likely to have an increase in OPSAT-Q CSS than patients aged ≥65 years (estimated odds ratio [OR] 1.70, 95% CI 1.35–2.13, *p* < 0.0001). Patients who reported stomach upset within 48 hours of taking their previous weekly bisphosphonate more than once a month at study entry were three times more likely to be more satisfied at the end of the study than patients who did not (87.3% vs. 69.5%; estimated OR, 2.98, 95% CI 1.52–6.50, *p* = 0.0026).

TABLE 3. DEMOGRAPHIC AND DISEASE CHARACTERISTICS IN INTENT-TO-TREAT POPULATION^a

Parameter	All patients (n = 1678)
Race	
White	1595 (95)
Black	44 (3)
Other	39 (2)
Age, years	
Mean ± SD	65.9 ± 9.67
Range	38–95
Body mass index, kg/m ² (n = 1673)	
Mean ± SD	25.8 ± 4.98
Range	13.6–50.4
Highest level of education	
Elementary school	22 (1)
Some high school	68 (4)
High school graduate/GED ^b	472 (28)
Some college	553 (33)
College graduate	375 (22)
Postgraduate degree	188 (11)
Current occupation	
Not working	1021 (61)
Working	656 (39)
Living environment, activity level	
Home, independent	1658 (99)
Home, with assistance	13 (<1)
Assisted living facility	6 (<1)
Nursing home	1 (<1)
Major risk factors for fracture ^c	
History of fractures as an adult	474 (28.2)
Low body weight (<58 kg)	474 (28.2)
History of fragility fracture in first-degree relative	335 (20.0)
Current smoker	151 (9.0)
Use of oral corticosteroid therapy for >3 months	83 (4.9)
None indicated	593 (35.3)
BMD status (primary diagnosis)	
Osteoporosis	1083 (64.5)
Osteopenia	595 (35.5)
Months since diagnosis, mean ± SD	
Osteoporosis (n = 1079)	58.8 ± 51.7
Osteopenia (n = 595)	38.7 ± 29.6
Taking osteoporosis/osteopenia medication	1678 (100)
Years of taking osteoporosis/osteopenia medication, mean ± SD (n = 1648)	2.8 ± 2.3
Responses to screening questionnaire	
Preference for monthly dosing	Yes: 1347 (80.3) No: 329 (19.6) Missing: 2 (0.1)
Stomach upset within 48h of dose with weekly bisphosphonate more than once a month	Yes: 89 (5.3) No: 1587 (94.6) Missing: 2 (0.1)
Missed three or more doses in last 3 months of weekly bisphosphonate	Yes: 141 (8.4) No: 1534 (91.4) Missing: 3 (0.2)

^aData are presented as number (%) of patients unless otherwise indicated. *n*, number of patients contributing to summary statistics. Percentages are based on *n* in the column header.

^bGED, general educational development (high school equivalency certificate).

^cA patient could have ≥1 risk factor.

TABLE 4. OPSAT-Q SCORES AT BASELINE AND AFTER 6 MONTHS OF MONTHLY ORAL IBANDRONATE TREATMENT IN INTENT-TO-TREAT POPULATION^a

	OPSAT-Q composite satisfaction score	OPSAT-Q ^b domain scores			
		Convenience	Quality of life	Overall satisfaction	Side effects
Baseline (scale 0–100)	80.1 ± 15.53	72.7 ± 22.18	78.5 ± 20.30	75.7 ± 21.82	93.3 ± 12.71
Month 6 (scale 0–100)	89.1 ± 15.15	88.3 ± 18.31	87.8 ± 20.17	87.8 ± 21.91	92.4 ± 14.24
Change from baseline	9.0 ± 20.80*	15.6 ± 27.73*	9.2 ± 26.69*	12.0 ± 31.03*	−0.9 ± 15.67**
Percent change from baseline	17.8 ± 44.54	41.3 ± 125.62	19.4 ± 58.82	30.5 ± 91.58	1.6 ± 30.88

^aMean ± SD.

^bOPSAT-QTM, Osteoporosis Patient Satisfaction Questionnaire.

* $p < 0.0001$; ** $p = 0.02$.

Patients who reported missing three or more doses of their previous weekly bisphosphonate in the past 3 months at study entry were two times more likely to be more satisfied than patients who did not (81.9% vs. 69.4%; estimated OR 1.82, 95% CI 1.13–3.04, $p = 0.0170$).

Preference

Of 1678 patients in the ITT population, after 6 months of treatment with monthly oral ibandronate, 87.0% (1460) completed the Pref-Q. Of the patients who completed the Pref-Q, 84.6% (1235) of patients preferred monthly treatment, 9.3% (136) preferred weekly treatment, and 6.1% (89) did not have a preference. Of patients who answered No to all three screening questionnaire questions, 68.1% (224 of 329 patients) indicated a preference for monthly ibandronate after 6 months of treatment.

The most common reasons cited for preferring either regimen were that it fits the patient's lifestyle better (patients who preferred monthly ibandronate 69.8%, weekly bisphosphonates 64.7%) and is easier to follow for a long period of time (monthly ibandronate 73.5%, weekly bisphosphonates 63.2%). Most patients thought that their preferred regimen was more convenient than the other regimen (monthly ibandronate 95.3%, weekly bisphosphonates 78.7%).

phosphonates 64.7%) and is easier to follow for a long period of time (monthly ibandronate 73.5%, weekly bisphosphonates 63.2%). Most patients thought that their preferred regimen was more convenient than the other regimen (monthly ibandronate 95.3%, weekly bisphosphonates 78.7%).

Compliance

Mean treatment compliance was high, with $96.0\% \pm 15.66\%$ (mean ± SD) of planned doses taken by patients who completed the study. Overall, 94.0% ($n = 1577$) of patients in the ITT population took at least five of the six planned doses.

Monthly reminder

Nearly half (44.8%) of the ITT population requested a monthly reminder to take their medication. Compliance was similar in the group of patients who requested a reminder and the group of patients who did not request a reminder (95.1% and 93.1% of patients, respectively, took at least five of the six planned doses of ibandronate).

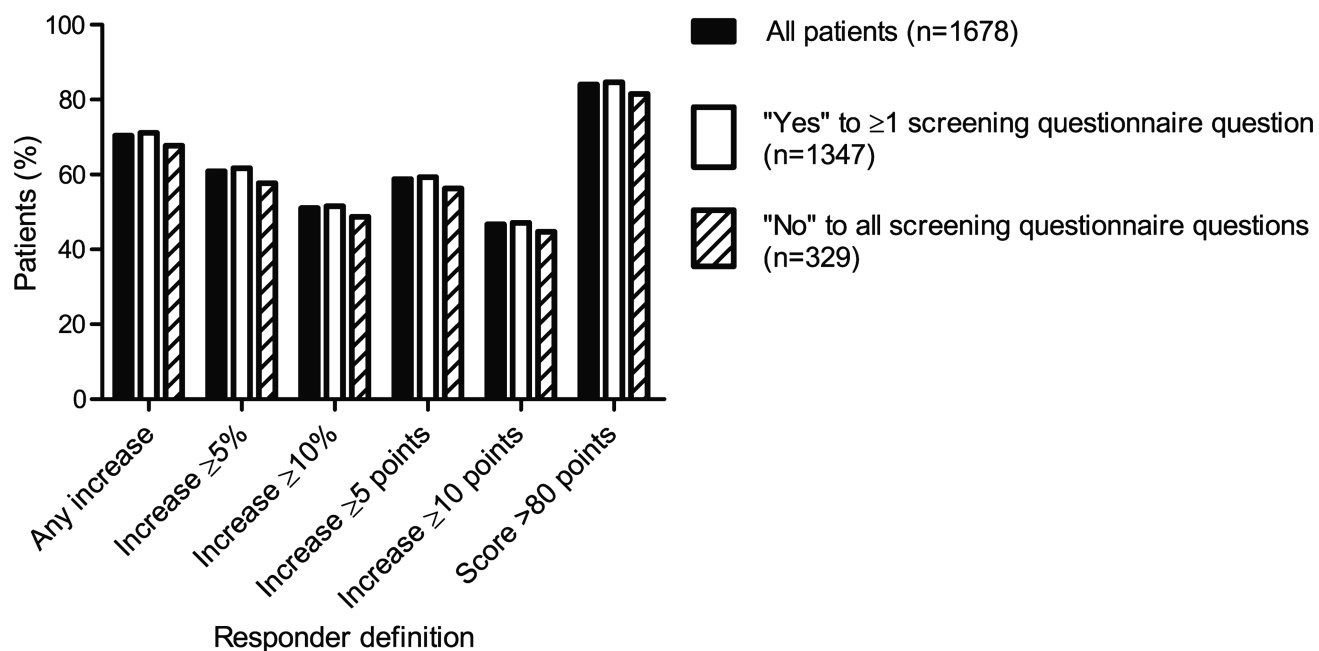


FIG. 2. Osteoporosis Patient Satisfaction Questionnaire (OPSAT-Q) satisfaction responder rates using various definitions of satisfaction response.

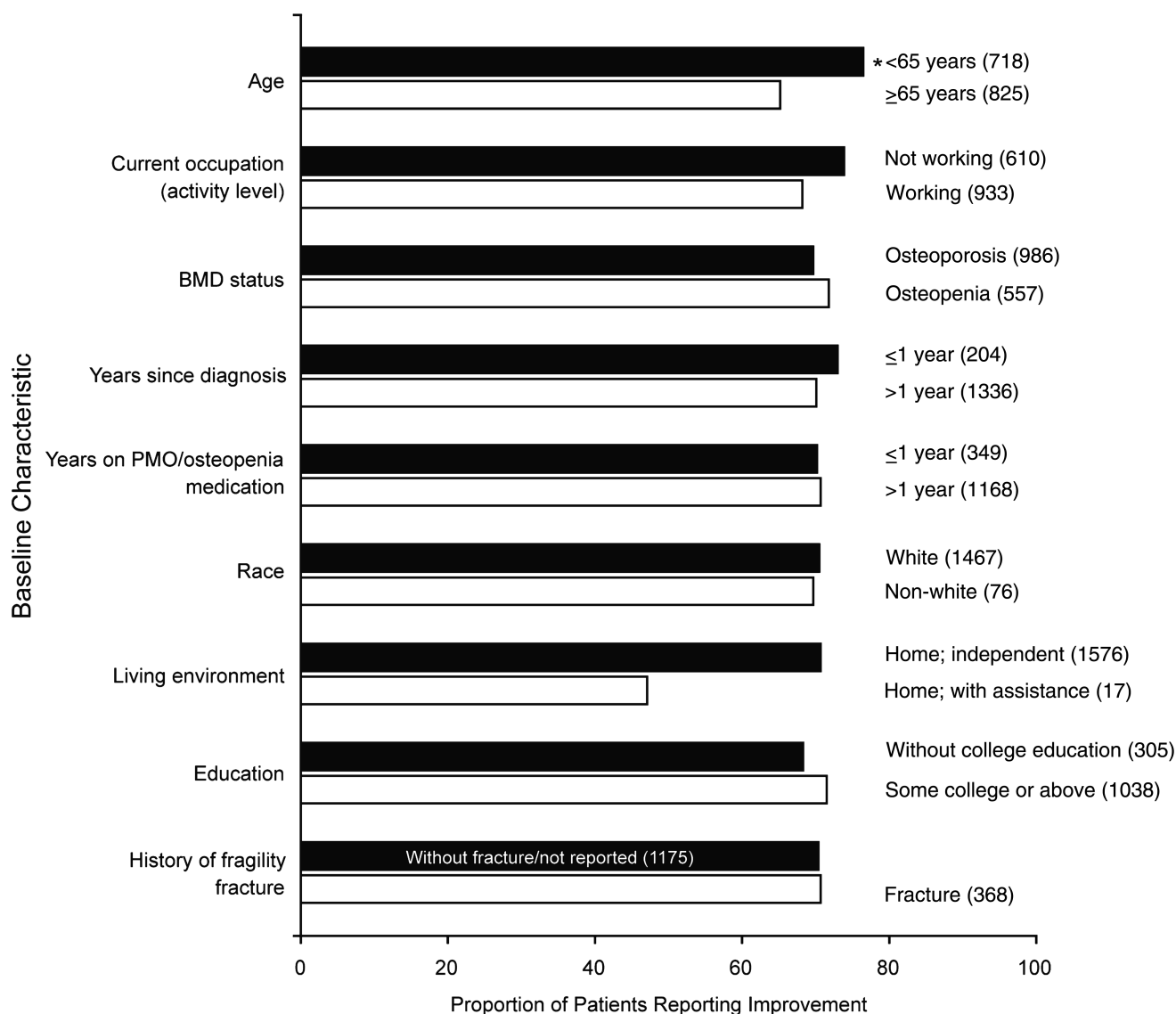


FIG. 3. Proportion of patients with improvement in Osteoporosis Patient Satisfaction Questionnaire (OPSAT-Q) composite satisfaction score at 6 months compared with baseline, by demographic and clinical characteristics. *Odds ratio = 1.7 (95% confidence interval 1.35–2.13); $p < 0.0001$. BMD, bone mineral density; PMO, postmenopausal osteoporosis.

Safety

In the safety population ($n = 1669$), the proportion of patients who reported at least one AE was 41.3% ($n = 689$) during the treatment phase. Forty patients (2.4%) had a fracture-related AE. Other AEs occurring with an incidence of $\geq 2\%$ were upper respiratory tract infection (3.2%, $n = 54$), dyspepsia (2.5%, $n = 42$), arthralgia (2.3%, $n = 39$), gastroesophageal reflux disease (2.2%, $n = 37$), diarrhea (2.2%, $n = 36$), and nausea (2.2%, $n = 36$). Most AEs were judged by the investigators to be mild to moderate in intensity. The proportion of patients who experienced AEs that were of severe intensity was 8% ($n = 133$). The most common severe intensity AEs were diarrhea (7 patients), upper abdominal pain (6 patients), and back pain, chest pain, and shoulder pain (5 patients each).

The proportion of patients with AEs assessed by the investigator as possibly or probably drug related was 11.3% ($n = 188$). The most common investigator-perceived drug-

related AEs were dyspepsia (1.9%, $n = 32$), gastroesophageal reflux disease (1.5%, $n = 25$), nausea (1.3%, $n = 21$), arthralgia (1.0%, $n = 17$), and diarrhea (0.8%, $n = 13$).

The overall incidence of serious AEs was 3.2% ($n = 54$). The most common serious AEs were chest pain (4 patients), atrial fibrillation (3 patients), breast cancer (3 patients), and syncope (3 patients). All serious AEs were judged by the investigators to be either unrelated or remotely related to ibandronate treatment.

Discussion

Ibandronate is approved for the prevention and treatment of postmenopausal osteoporosis¹⁰ and is the first bisphosphonate available for use in a monthly dosing regimen. The objective of CURRENT was to assess patient satisfaction with monthly ibandronate in a population of former weekly bisphosphonate users.

The mean level of satisfaction after treatment with monthly ibandronate was greater than at baseline (OPSAT-Q mean CSS 89.1 at month 6 vs. 80.1 at baseline). A total of 70.4% of patients had improved satisfaction scores following 6 months of monthly ibandronate treatment, despite relatively high baseline satisfaction scores. Patients <65 years were more likely to be satisfied than patients ≥ 65 years. Patients who reported previous gastrointestinal intolerance or noncompliance were more likely to be satisfied after 6 months of monthly ibandronate treatment than those who did not. Monthly ibandronate was generally well tolerated, and all serious AEs reported were considered by the investigators to be unrelated or remotely related to ibandronate treatment.

Preference for monthly oral ibandronate vs. a weekly bisphosphonate was also documented in two independently conducted multicenter clinical trials, Boniva Alendronate Trial in Osteoporosis (BALTO) I and II, in which patients were randomized to receive monthly ibandronate or weekly alendronate for 3 months or 12 weeks, respectively, using a crossover design.^{11,12} In these two studies, the Pref-Q was completed at the conclusion of the two crossover periods. The majority of patients preferred the monthly dosing schedule (71.4% of patients expressed a preference in BALTO I and 70.6% in BALTO II) and found it more convenient (74.6% of patients who expressed a preference in BALTO I and 76.6% in BALTO II).^{11,12} The most common reasons given for patient preference in both studies were ease of following the treatment for a long time and the ability of the regimen to fit better into the patient's lifestyle, as was seen in the CURRENT study.

Potential limitations of the present study include its open-label design and the possible effect of study participation itself on satisfaction. The open-label study design was necessary given the objectives of the study; however, it is possible that patients more likely to prefer monthly dosing were also more likely to enter the study, consistent with the high proportion of patients expressing a preference for monthly dosing on the screening questionnaire. However, prior use of a weekly bisphosphonate before beginning a monthly bisphosphonate is likely to be representative of the experience of many patients in a clinical setting.

Compliance with monthly ibandronate in this study was high. This may have been influenced by such factors as selection bias toward patients more likely to take osteoporosis medication, as indicated by the high baseline level of compliance with weekly bisphosphonates, and the effect of trial participation on patients' inclination to continue taking the drug. Compliance was assessed by recording drug dispensed and returned, although this does not necessarily indicate that the medication was taken as prescribed and may overestimate actual compliance with treatment. As noted previously, there was a high level of baseline satisfaction and compliance in this study. Therefore, these results may not be applicable to a population of women in whom baseline satisfaction and compliance are low. Nevertheless, in spite of apparently good compliance and a low rate of gastrointestinal side effects with weekly dosing based on screening questionnaire responses and satisfaction with weekly bisphosphonate treatment based on the baseline OPSAT-Q CSS, satisfaction scores significantly improved after 6 months of monthly ibandronate treatment. Thus, this study may provide useful information on how patients receiving a weekly bisphosphonate might perceive monthly ibandronate treatment after switching. The duration

of this study was relatively short at 6 months. The high level of satisfaction, compliance, and preference for monthly ibandronate observed over 6 months may not correspond to a high level of satisfaction, compliance, or preference in patients treated for longer periods.

Finally, the study population was 95% Caucasian, and 94% had at least a high school diploma or its equivalent. The results of this study may not be applicable to women of other races or ethnicity or of different educational backgrounds.

A patient's preference for one treatment over another addresses his or her reaction to the treatment.⁶ Preference may impact patient satisfaction¹³ and, ultimately, compliance with treatment. Compliance with treatment has been shown to be associated with reduced fracture risk in osteoporosis^{7,14,15} and is, therefore, an important treatment goal for osteoporosis. The results of this study suggest that monthly ibandronate is associated with a high level of patient satisfaction with oral bisphosphonate treatment in general and specifically in patients who were previously gastrointestinal intolerant or missed doses of their previous weekly bisphosphonate therapy. This may prove helpful in encouraging patients to continue bisphosphonate treatment and, thus, realize its benefits in reducing fracture risk associated with osteoporosis.

Results from this trial add to our understanding of patient satisfaction with bisphosphonate treatment. They suggest that patients who switch from a weekly regimen of alendronate or risedronate to a monthly regimen of ibandronate may experience increased satisfaction with their bisphosphonate treatment based on data from a validated self-reported satisfaction questionnaire.

Conclusions

Data from this large multicenter trial of postmenopausal women, previously receiving a weekly bisphosphonate, showed that the majority of patients reported improved satisfaction when switched to monthly ibandronate even though baseline satisfaction was high. A greater proportion of patients preferred monthly oral ibandronate to their prior weekly bisphosphonate treatment after 6 months of therapy.

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The CURRENT study is registered through the International Federation of Pharmaceutical Manufacturers and Associations trial portal (IFPMA, www.ifpma.org/clinical_trials.html). The protocol number is ML 18056.

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