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Sponsor/company:	**sanofi-aventis**	**ClinialTrials.gov Identifier:**	
		Study Code:	**HMR4003B_4031**
Generic drug name:	**Risedronate**	**Date:**	**November 9th, 2006**

Title

Point-Of-care device and Actonel® once-a-WEek dosing satisfaction tRial (POWER study): Impact of NTx Point-Of-Care (POC) device on subject satisfaction with Actonel® 35 mg once-a-week treatment—a multicentre prospective open label randomized controlled community practice-based study.

Investigator(s), study site(s)

Multicentre: 445 centres in Canada

Study duration and dates	The study took place between 27 February 2003 and 18 November 2004.	Phase	IV

Objectives

Primary: The objective of this study was to compare the subject satisfaction rating in women treated for postmenopausal osteoporosis with Actonel® 35 mg Once-a-Week for 24 weeks, and receiving feedback information after 12 weeks of treatment (based on bone resorption marker results using the NTx Point-Of-Care [POC] device), to similar women monitored as per regular clinical practice

Secondary:

- To compare subject satisfaction with Actonel® 35 mg Once-a-Week in the following subject subgroups: those previously treated for osteoporosis with biphosphonates (alendronate, etidronate), hormone replacement therapy (estrogen, estrogen-related drugs, progesterone, subcutaneous estrogen implant), raloxifene, fluoride, or calcitonin within the past 2 years vs. those previously non treated.
- To document bone marker (NTx levels) response to Actonel® 35 mg Once-a-Week after 12 weeks of treatment.
- To evaluate the correlation between measures of subject satisfaction with Actonel® 35 mg Once-a-Week and NTx bone marker results after 12 weeks of treatment.

Study design

This was a multicentre, prospective, open-label, randomized, controlled community practice-based study in women with postmenopausal osteoporosis. Subjects were to be treated with Actonel® 35 mg Once-a-Week for 24 weeks. All subjects attended a screening/baseline visit and a 24-week visit. In addition, approximately half of the subjects were randomized to return for a 12-week visit to get feedback about the effectiveness of treatment based on results of the NTx-POC test (compared with a baseline measure). All subjects completed a Subject Satisfaction Questionnaire at the final 24-week visit.

Number of subjects planned

A total of 2400 subjects were to be enrolled into the study.

Inclusion criteria

The study included women diagnosed with postmenopausal osteoporosis who had either never been treated for osteoporosis, or, had been treated previously but discontinued prior to enrolment into the study due to lack of effect, or intolerance, or health concerns (e.g. hormone replacement therapy).

Treatments

Each subject received risedronate 35 mg tablets once weekly (Actonel® 35 mg Once-a-Week [Lot 379277]). Concomitant use of calcium and vitamin D directed by the investigator was allowed.

Efficacy data

Efficacy data included Subject Satisfaction Questionnaire scores and NTx-POC values.

Safety data

Safety data were adverse events reported by the subject or noted by the investigator.

Statistical procedures

The Intent-to-Treat (ITT) population included all randomized subjects. The Completer population consisted of all ITT subjects who had a final visit within the window of the 24-week visit and was used to confirm the ITT results. The Safety population was defined as those subjects who received at least one dose of study medication.

For the primary efficacy analysis, a Cochran-Mantel-Haenszel procedure controlling for pooled site was use to compare the percentage of subjects satisfied (mean total score on Subject Satisfaction Questionnaire of at least 3.5) between the NTx and No NTx groups. Consistency of effect was explored using logistic regression. Analysis of variance (ANOVA) was used to analyze total satisfaction score and additional visits related to osteoporosis. Descriptive statistics were calculated for baseline and change from baseline values for NTx. The association between subject satisfaction scores, NTx values, and additional visits was assessed with multiple linear regression and correlation.

Interim analysis

Baseline data for this study were presented at the American Society for Bone and Mineral Research (ASBMR) meeting in October, 2004. No on-treatment data were analyzed prior to database lock.

Results - Study subjects and conduct

A total of 2433 subjects were screened and randomized into the study; 1202/2433 (49.4%) subjects were randomized to the NTx study group and 1231/2433 (50.5%) subjects were randomized to the No NTx group. When subjects were divided into strata according to previous treatment, there were 1225/2433 (50.3%) subjects in the Naïve stratum (620/1225 (50.6%) NTx subjects and 605/1225 (49.4%) No NTx subjects) and 1208/2433 (49.7%) subjects in the Treated stratum (582/1208 (48.2%) NTx subjects and 626/1208 (51.8%) No NTx sujbects).
Altogether, 253/2433 (10.4%) subjects (138/1202 (11.4%) NTx subjects and 115/1231 (9.3%) No NTx subjects) were withdrawn from the study for the following reasons: adverse event (124 subjects); did not wish to continue (48 subjects); other reason (42 subjects); lost to follow-up (34 subjects); and death (5 subjects).

All subjects received Actonel® 35 mg Once-a-Week. The mean (± SD) duration of study drug was 165 ± 47 days, with a minimum of 1 day and a maximum of 385 days.

The mean age of study subjects was 68.4 years, with a minimum of 40 and a maximum of 100 years. The NTx and No NTx study groups appeared to be well balanced within each stratum.

Results – Efficacy

The primary efficacy analysis compared the percent of subjects satisfied (defined as mean total score for satisfaction questionnaire of 3.5 or higher) between the NTx and No NTx groups. There was no statistical difference between study groups: 95.1% of the NTx group was satisfied and 95.0% of the No NTx group was satisfied (P = 0.9587). Consistency of effect analysis showed statistically comparable results in those subjects 70 years or older versus those younger than 70 years of age, and in those subjects in the Naïve versus the Treated stratum.

Secondary analyses revealed that there was no statistically significant difference in adjusted mean total satisfaction scores between the NTx group (5.34) and the No NTx group (5.28; P = 0.1723).
However, in a post-hoc analysis, a small but statistically significant difference between study groups was observed when the threshold score was raised to 5.5: 65.6% of the NTx group were satisfied versus 61.2% of the No NTx group (P = 0.0479).
Treatment effectiveness was indicated by a significant decrease in absolute NTx values from baseline to the Week 12 measure in both the Naïve and Treated study strata (P = 0.0001). At endpoint, 86.8% of the subjects in the Naïve stratum, and 90.7% of subjects in the Treated stratum had premenopausal NTx values.
There did not appear to be any significant correlation between NTx values and total satisfaction score or the number of additional visits for osteoporosis.

Results – Safety

A total of 181/2433 (7.4%) subjects reported adverse reactions during the study; most were gastrointestinal disorders (112/2433 subjects; 4.6%) or musculoskeletal and connective tissue disorders (45/2433 subjects; 1.8%). The most frequent adverse reaction was arthralgia (18/2433 subjects; 0.7%), followed by abdominal pain, diarrhoea, and dyspepsia, all reported in 15/2433 (0.6%) subjects.

Four subjects had five serious adverse reactions, including gastritis, fecaloma, angina pectoris, vertigo and neck pain. All four subjects recovered from these reactions and no subjects died due to an adverse reaction. A total of 100 subjects discontinued study medication due to an adverse event; most due to gastrointestinal disorders (61 subjects) or musculoskeletal and connective tissue disorders (21subjects). Overall, the adverse events observed in this trial were consistent with those previously reported for the marketed medication (Actonel Once-A-Week).

Date of Report September 29th 2006