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Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NA
		Study Code :	HMR4003B_4035
Generic drug name:	Risedronate Sodium	**Date :**	04/May/2007

Title	A Multicenter, Prospective, Randomized, 2-Way Crossover, Open-Label Study in Postmenopausal Women with Osteoporosis Examining Subject Satisfaction and Compliance when Actonel® (Risedronate) is Administered 35 mg Once A Week or 5 mg Once Daily
Study duration and dates	The first subject was enrolled on 20 November 2003, and the last subject completed the study on 22 November 2004.
Investigator(s), Study site(s)	Multi-national (Korea and Taiwan), Multi-center (7 centers) clinical trial Coordinating investigator: Dr. Park, Il Hyung Kyung Pook University Hospital
Phase	IIIb in Taiwan / IV in Korea
Objectives	- **Primary objective** : To compare subject satisfaction of once a week dosing of 35 mg Actonel® to once daily dosing of 5 mg Actonel® in postmenopausal osteoporotic women. - **Secondary objective** : To measure compliance (50 % drug taken) and persistence. A subject administered questionnaire and tablet counts at 12 and 24 weeks would assess persistence and compliance.
Study design	A multicenter, prospective, randomized, 2-way crossover, open-label
Number of subjects	Total No of enrolled Subjects: 262 Treatment duration with Actonel®: 216 Total No of subjects included in ITT : 199 Total No of subjects included in PP : 185 Total No of subjects included in safety analysis: 216
Inclusion criteria	1. Ambulatory, women between the ages of ≥55 and ≤80 years, 2. Five years or greater postmenopausal who presented with a diagnosis of postmenopausal osteoporosis based on standard clinical practice criteria. 3. Be able and willing to participate in the study and provide written informed consent. 4. Subjects had to discontinue bisphosphonates, calcitonin, fluoride, glucocorticoids (≥ 5 mg prednisone or equivalent per day) and hormone replacement therapy including estrogen-related compounds at least 6 months prior to randomization.

	Other concomitant medications should be kept to a minimum, but if the drugs were considered necessary for the subject's welfare and were unlikely to interfere with study medication they might be given at the discretion of the Investigator.
Exclusion Criteria	1. Had a history of cancer within the past 5 years. Relatively benign skin malignancies, such as basal cell carcinoma or squamous cell carcinoma, were not exclusion if the subject had been in remission for at least 6 months prior to enrollment. 2. Diagnosis of hypocalcaemia, hyperparathyroidism, and hyperthyroidism. 3. History of alcohol and/or drug abuse. 4. Subjects would be excluded for active gastrointestinal disease that might interfere with absorption or with ability to swallow an oral medication. 5. Subjects would also be excluded for serious concurrent illness that would interfere with their ability to participate in the trial. 6. Excluded medications: bisphosphonates, calcitonin or fluoride or hormone replacement therapy within the last 6 months. 7. Known hypersensitivity to bisphosphonates and/or excipients 8. Abnormal laboratory parameters, which were clinically relevant according to the Investigator (including renal insufficiency; creatinine clearance < 30 mL/min) 9. Evidence of clinically significant psychiatric disorder, which in the opinion of the Investigator and sponsor would prevent the subject from completing the study. Mental condition rendering the subject unable to understand the nature, scope, and possible consequences of the study 10. Likelihood of requiring treatment during the study period with drugs not permitted by the study protocol 11. Subject unlikely to comply with protocol, e.g., uncooperative attitude, inability to return for follow-up visits, and unlikelihood of completing the study. 12. Subjects previously treated with the investigational product within the last 30 days will not be enrolled in this study.
Treatments	Subjects were randomized (1:1) to receive (orally) either Actonel® 5 mg once daily or Actonel® 35 mg once a week for 12 weeks and then followed by a crossover to the other treatment for 12 weeks. They also received throughout the study calcium 500 mg + vitamin D 125 IU (orally, qd).
Efficacy Data	- Primary Endpoint: Measurement of subject satisfaction of once a week 35 mg Actonel® and once daily 5 mg Actonel® A subject administered questionnaire at 12 and 24 weeks assessed satisfaction. - Secondary Endpoints: The subjects' compliance and persistence on treatment. Compliance as defined by more than 50% of the drug taken (by tablet count) during each Actonel ® treatment period. Persistence at week 12 and 24 was defined as continuing Actonel® treatment.
Safety Data	Adverse events Laboratory measurements
Statistical Procedures	Subject preference of 'once a week dosing' of Actonel® 35 mg and 'once daily dosing' of Actonel® 5 mg were compared ('once daily dosing'/'once a week dosing'/'no preference') and the relative preference for each dosage regimen was estimated with a 95% confidence interval.
Interim analysis	No interim analysis was performed.

Results	*Subjects demographics* The mean age of subjects receiving the study treatment was 65.7 in the "Weekly to Daily" group, and 65.8 in the "Daily to Weekly" group. The mean body weight was 54.2kg in the "Weekly to Daily" group, and 54.6 kg in the "Daily to Weekly" group. There was no significant difference between the two groups ($p>0.05$). *Results- preference, compliance and persistence* 1. Preference The primary efficacy variable in this study was the preference obtained by the questionnaire. The study result indicated that the preference of 'once a week dosing' regimen of Actonel® 35mg was 2 times greater than that of 'once daily dosing' regimen of Actonel® 5 mg (once daily dosing: 25.1% and once a week dosing: 52.8%, and p-value<0.0001). 2. Compliance and persistence The overall compliance and persistence for Actonel did not show statistical difference between the 'two types of dosing interval (p-values of the 50% and 80% compliance are 1.0000 and 0.0522 respectively; p-values of the persistence under each of the two assumptions are 1.000 and 0.4669). The compliance for the 500 mg calcium + 125 IU vitamin D (Oscal 500D®) taken once daily was less than that of the once a week dosing. However, since the level of compliance and persistence were both very high in both crossover treatment groups, no significant difference was found between the two dosing regimens. *Results- Safety* Safety was evaluated by analyzing adverse events occurring after the administration study initiation, hematology/biochemistry laboratory values during the study, and vital signs. Adverse events occurring after the first dose were reported by 42 subjects (38.2%) in the "Weekly to Daily" crossover treatment group, and 32 subjects (30.2%) in the "Daily to Weekly" crossover treatment group. Alternatively, these adverse events were reported by 48 subjects (22.8%) during the 'once daily dosing' regimen and 42 subjects (20.2%) during the 'once a week dosing' regimen. There was no statistically significant difference between the "Weekly to Daily" and the "Daily to Weekly" crossover treatment group. The most frequently reported adverse events (TEAE) that occurred after the administration of the first dose of the study drug was gastrointestinal disorder. The reported adverse events, which were suspected to be related to the study drugs by the physician, included by 15 subjects (13.6%) in the "Weekly to Daily" crossover treatment group, 11 subjects (10.4%) in the "Daily to Weekly" crossover treatment group, 13 subjects during the 'once daily dosing' regimen and 13 subjects during the 'once a week dosing' regimen. All serious adverse events were determined to be unrelated to the study drug, and none of them led to the withdrawal of treatment or death.
Date of report:	10-May-2006