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Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00453492
		Study Code:	HMR4003B_4036
Generic drug name:	Risedronate sodium	**Date:**	10/Mar/2008

Title of the study:	A phase IV, Open label, double-crossover, randomized, prospective, multicenter study comparing patient satisfaction and compliance between once weekly use of Actonel®(Risedronate) 35mg and that of once daily use of 5 mg among postmenopausal osteoporotic women patients
Investigator(s):	Multicenter study Coordinator investigator: Prof.Dr. Refik Tanakol, Istanbul University, Istanbul Medical School Department of Endocrinology and Metabolic Diseases Istanbul- Turkey
Study center(s):	Multicenter study (12)
Publications (reference):	NA

Study period: Date first **patient** enrolled: July 2004 Date last **patient** completed: Sep 2005	**Phase of development:** Phase IV

Objectives:	Primary objective: To compare patient satisfaction in postmenopausal women with osteoporosis treated with Actonel® (Risedronate) 35 mg once a week or 5 mg once daily. Secondary objectives: To measure patient compliance (50% compliance to treatment) and continuity to treatment (and urinary NTx). Patient compliance and continuity to treatment were evaluated with patient questionnaire completed on 12th and 24th weeks and the number of tablets returned. The effects of Actonel® on bone resorption were evaluated with the change in urinary NTx in 12th and 24th weeks compared to baseline values (Only for patients who had not received osteoporosis treatment previously).

Methodology:	**Calendar for collection and sampling of urine** The patients will be instructed to collect samples of their second urine on the morning of starting visit (Between 05:00-09:00 AM), 3rd and 4th visits (24th week), and also on the days preceding these visits (Clinical visit, -1 day). Six (6) urine samples will be collected for each patient during the study. The patients will be instructed to fast from 23:00 PM, on the night preceding the collection of the urine sample. **NTx Point-of-Care** The measurement of Urine NTx will not be made at the side of the patient. Please collect 10 ml each, separately from the two samples of urine collected form the patient via a straw. Mix those in a sterile container prior to the use of a specified part for the NTx Point of Care instrument. The results can be read from the instrument after 5 minutes. Please record the results on the CRF. Please record the results of the NTx Point-Of-Care instrument along with patient and visit numbers, and if possible save them in a computer program for confirmation (For Guidelines See Appendix C: Markers of Bone Turnover, NTx Chapter, page 60). **Data for Compliance** After the patient has left the study Center, the study drug returned by the patient (both Actonel and Calcium + Vitamin D) will be counted and the result recorded on CRF.		
Number of patients:	Planned: 290 subjects	Randomized: 296 subjects	Treated: 296 subjects
Evaluated:	225 subjects	Safety: NA	Pharmacokinetics: NA
Diagnosis and criteria for inclusion:	Female patients aged 50-80 years, in postmenopausal period for at least 5 years and with a clinical diagnosis of postmenopausal osteoporosis were included to the study.		
Investigational product:	The patients will be randomized to receive either at the starting visit (1:1), and then they will be enrolled to the other arm of treatment for the next 12 weeks. There will not be washout period for the drug between drug changes. Standard guidelines of use for Actonel are as follows: taken at least 30 minutes before the first meal or drink of the day (except drinking water), or at any time of the day with at least an interval of 2 hours from any meal or drink and at least 30 minutes before retiring to sleep. Study drug should not be taken with any other drink than normal drinking water. Dairy products and other products containing calcium (for example: antacids) may disturb the absorption of the study drug and therefore should not be taken simultaneously with the drug. Additionally, the drug should be taken with a glass of normal drinking water (at least 4-oz/ 120 ml) in upright position and the patients should not lie down during the first 30 minutes after the consumption of the drug.		
Dose:	Actonel 35 mg once a week or Actonel 5 mg once a day for 12 weeks		
Administration:	Oral administration in both treatment regimens		
Duration of treatment: 24 weeks		Duration of observation: 24 weeks	
Reference therapy:	NA		
Dose:	NA		
Administration:	NA		
Criteria for evaluation:			
Efficacy:	Urinary NTx levels are accepted as an indicator of bone resorption		
Safety:	NA		
Pharmacokinetics:	NA		
Pharmacokinetic sampling times and bioanalytical methods:	NA		

Statistical methods:	Data of two dose regimens were compared using repeated measures ANOVA except the 8th question in Patient Satisfaction Questionnaire that was answered in 24th week. The compliance and continuity between dose regimens were compared using McNemar's test. Statistical significance level was defined as $p<0.05$.
Summary:	296 subjects were randomised to the study with intend to treat protocol. 71 subjects discontinued during the trial and they were excluded from the analysis. The analysis was performed on 225 subjects. The mean age of the 225 patients was 62.0±6.9 years. The age of the 110 patients initially treated with once a week dosing was not statistically different from that of the 115 patients who started with once a day dosing regimen (61.3±6.4 and 62.6±7.4 years, respectively, p=0.30).
Efficacy results:	Of the patients under weekly dosing regimen, 20 (27.8%) and 15 (26.3%) were extremely pleased with the ease of taking Actonel® in Weeks 12 and 24, respectively. Among the patients under daily dosing regimen, 12 (19.7%) were extremely pleased with the ease of taking Actonel® in Week 12, while this ratio increased to 20 (30.8%) at the end of Week 24. Overall, 35 (27.1%) patients under weekly dosing regimen were extremely pleased with the ease of taking Actonel®, while the number of extremely pleased patients was 32 (25.4%) in the daily dosing regimen. The overall convenience of taking Actonel® was slightly higher among the patients under weekly dosing regimen; 32 (25.6%) patients under weekly dosing regimen and 26 (21.8%) patients under daily dosing regimen were extremely pleased with the medication. In weekly dosing group, the ratio of extremely pleased patients decreased from 22 (31.4%) in Week 12 to 10 (18.2%) in Week 24. In daily dosing regimen, this ratio increased from 10 (17.2%) in Week 12 to 16 (26.2%) in Week 24. Means of basal urinary NTx levels in the daily and the weekly dosing groups were 100.4±162.2 (min: 2, and max: 752) and 120.9 (min: 2, and max: 889), respectively. Urinary NTx levels indicating bone resorption were similar in daily and weekly dosing regimen of Actonel®. There was a statistically significant difference between Week 12 and Week 24 in once a week dose group (p=0.003; Wilcoxon test).
Safety results:	Thirty-nine patients (intend-to treat protocol) experienced 56 adverse events, mostly with mild or moderate severity, during the study. Weekly and daily dosing regimens of Actonel® were not different regarding the frequency and the outcomes of adverse events (AEs). The relation of the two dosings to AEs and the resulting clinical decisions were also comparable, however, the intensity of the AEs was significantly different between the two regimens. Overall, weekly dosing regimen was better tolerated than daily dosing regimen according to physicians' general impressions.
Pharmacokinetic results:	NA
Date of report:	06-March-2008