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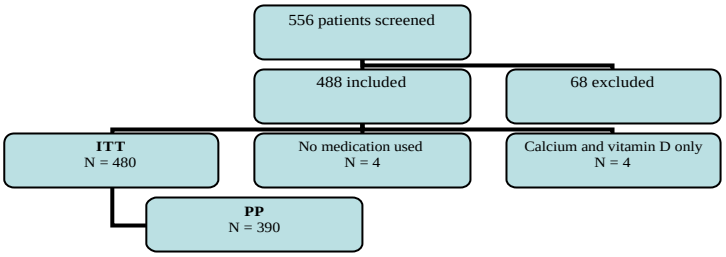
Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT
		Study Code:	RISED_L_01054
Generic drug name:	Risedronate Sodium	**Date:**	03/Mar/2008

Title of the study:	Multicenter and prospective study to determine the satisfaction with risedronate sodium 35mg once a week using biochemical markers of bone as a control, in postmenopausal women with osteoporosis. RISED_L_01054		
Principal Investigator(s) name or study coordinator:	Coordinating investigator: Cesar Eduardo Fernandes ISBEM – Instituto de Saúde e Bem Estar da Mulher – Avenida Indianópolis, nº 2700 - Planalto Paulista – São Paulo – SP – Brazil		
Study center(s):	Multicenter studies (7 BR sites)		
Publications (reference):	None (in submission)		
Study period: Date first patient enrolled: 03-Nov-2004 Date last patient completed: 24-May-2005		**Phase of development:** Phase IV	
Objectives:	Primary: To evaluate the patient satisfaction with the weekly formulation of risedronate sodium 35mg for the postmenopausal osteoporosis treatment. Secondary: To evaluate the risedronate sodium efficacy in the reduction of serum levels of CTx, after 3 months of treatment, in women postmenopausal osteoporosis.		
Methodology:	Multi center, open label, non-controlled study.		
Number of patients:	Planned: 500	Randomized: NA	Treated: 480
Evaluated:	Efficacy: 480	Safety: 488	
Diagnosis and criteria for inclusion:	Women with postmenopausal osteoporosis, aged between 55 and 70 years old, confirmed by densitometry and/or x-ray (bone mineral density and lumbar spine or femur neck T-score = - 2.5 in the referred date or a previous densitometry in the last 12 months or some evidence of vertebral fracture in the x-ray).		
Investigational product: Dose: Administration:	Risedronate sodium 35mg PO, Once a week		
Duration of treatment: 12 weeks		**Duration of observation:** 12 weeks	

Reference therapy:	NA
Dose:	NA
Administration:	NA
Criteria for evaluation:	
Efficacy:	The proportion of patients who evaluate the treatment (using a satisfaction questionnaire) as “excellent”, “good”, “satisfactory”, “bad” or “very bad”. The proportion of patients who evaluate the gastrointestinal tolerability (using a satisfaction questionnaire), at the end of the treatment, as “no new digestive symptoms”, “worsening of previous digestive symptoms”, “arise of new digestive symptoms”. The decrease in mean values of serum CTx from baseline to the end of study.
Safety:	Adverse events reported by the patient or noted by the investigator.
Statistical methods:	It was defined the Intent to Treat Population, compound by all patients who received at least one dose of risedronate. From this population, all patients who did not present any relevant protocol violation were included in the Per Protocol Population (PP). The efficacy analyses were done for both ITT and PP populations. The overall opinion of the patients about the treatment and about the gastrointestinal tolerability was evaluated using descriptive methods: frequency table. The efficacy analyses concerning the comparison of the serum CTx values at baseline and at the end of treatment was performed using a t-student test for paired samples, with a significant level of 5%. All 488 patients enrolled to the study were included in the safety analyses. Only descriptive methods were used to adverse events occurrence.

Summary:	A total of 556 postmenopausal women were screened, with 488 enrolled. At least one dose of risedronate was used by 480 patients (98.4%), with 81% completing the full 12 weeks of treatment and follow-up assessment (N = 390). Two patients did not use risedronate after experiencing AEs from calcium and vitamin D. The remaining six patients not receiving risedronate withdrew their consent prior to initiation of bisphosphonate treatment.  Within the ITT population, the mean age was 63.0 ± 3.8 years, with a range of 55 to 69 years. Most patients had at least one osteoporosis risk factor: weight <57 kg (N = 177, 36.9%), family history of osteoporosis (N = 159, 33.1%), former smoker (N = 96, 20.0%), current smoker (N = 59, 12.3%), or history of fracture with minor trauma before age 40 (N = 30, 6.3%). At least one risk factor was present for 352 women (73.3%), at least two risk factors in 139 (29.0%), and three or more risk factors in 30 (6.3%). All ITT patients had osteoporosis confirmed by diagnostic testing: bone densitometry in 479 and X-rays in one. Average group BMD of the lumbar spine was 787.4 ± 102.1 g/m2 (range: 304-1222 g/m2). Average group BMD of the femoral neck was 725.1 ± 106.0 g/m2 (range: 100-1079 g/m2). Reduced stature was observed in 267 patients (55.6%) and about 15% of the patients had already undergone some prior treatment for osteoporosis. Concerning ITT population, 173 patients (36.0%) missed doses of risedronate over the full 12 weeks of treatment due to forgetfulness. Among patients missing doses, 141 patients (81.5%) skipped treatment once or twice during the treatment period, with 90 (52.0%) of these patients taking the missed medication dosage on an alternative day of the same week.

Efficacy results:

Most of the patients (56.7%) considered the treatment as "Good". The treatment was considered "Excellent" by 35% of the patients and "Satisfactory" or "Bad" for about 7%. Concerning gastrointestinal tolerability, most of the patients (88%) have reported no new digestive symptoms (stomachache, burning, nausea and/or vomits).

From the total number of patients, 6 (1.2%) have not filled the satisfaction questionnaire due to lost of follow-up or consent withdrawn.

The results in both PP and ITT populations were very similar (Table 1).

Table 1: Overall treatment evaluation (satisfaction questionnaire) – ITT and PP Populations

Questions	ITT N=480	PP N=390
Overall evaluation of the treatment		
Excellent	168 (35.0%)	139 (35.6%)
Good	272 (56.7%)	223 (57.2%)
Satisfactory	27 (5.6%)	20 (5.1%)
Bad	07 (1.5%)	02 (0.5%)
Very bad	-	-
Not answered [1]	06 (1.3%)	06 (1.5%)
Overall evaluation of the gastrointestinal tolerability		
No new digestive symptoms	424 (88.2%)	346 (88.7%)
Worsening of previous digestive symptoms	17 (3.5%)	13 (3.3%)
Arising of new digestive symptoms	34 (7.1%)	25 (6.4%)
Not answered [1]	06 (1.2%)	06 (1.5%)

[1] Patients 82 and 91 from Center 1; Patients 16, 112 and 125 from Center 2 – Lost of follow-up;
Patient 55 from Center 5 – Consent withdrawal.

In the ITT population, the mean values of serum CTx were 0.42 at baseline and 0.16 at end of treatment. The decrease after risedronate use was statistically significant ($t=29.67$; $p<0.0001$). In the PP population, the results were very close to the observed in ITT population (Table 2).

Table 2: Serum CTx results - ITT and PP Populations

Serum CTx	ITT	PP
Baseline (Bas)	**N=480**	**N=390**
Mean ± SD	0.419 ± 0.234	0.413 ± 0.233
Median	0.39	0.39
Min-Max	0.03 – 1.44	0.03 – 1.44
End of Treatment (EOT)	**N=473**	**N=383**
Mean ± SD	0.158 ± 0.171	0.152 ± 0.169
Median	0.10	0.09
Min-Max	0.01 – 1.08	0.01 – 1.08
CTx $_{Bas}$ – CTx $_{EOT}$	**N=473**	**N=383**
Mean ± SD	-0.262 ±	-0.262 ± 0.196
Median	-0.25	-0.25
Min-Max	-0.95 – 0.78	-0.95 – 0.78
t-test	t= -29.67	t = -26.18
H_0: mean CTx_{BAS}-mean $CTx_{EOT}=0$	p < 0.0001	p < 0.0001

Safety results:	From the total number of patients enrolled to the study, 116 (23.8%) have reported some adverse event (AE) and 59 (12.1%) have presented at least one event considered as related to the risedronate intake. Six patients (1.2%) have reported a serious adverse event, although none of them has been considered as related to the study medication (Table 3). Table 3: Patients reporting any adverse event. The most commonly reported AEs were: non-specific aches (5.9%), abdominal pain (5.3%), nausea (2.9%), diarrhea (1.8%), constipation (1.2%) and dizziness (1.0%).
Date of report:	28-Dec-2007

Adverse event descriptions	Nº of patients (N=488)	Nº of events
Any	116 (23.8%)	160
Related to risedronate	59 (12.1%)	78
Serious	06 (1.2%)	06
Serious and related to risedronate	-	-
Causing death	-	-
Related to risedronate and causing	-	-
Leading to treatment withdrawal	10 (2.0%)	14
Related to risedronate and leading to treatment withdrawal	03 (0.6%)	03