Rates and reasons for lack of persistence with anti-osteoporotic drugs analysis of the Campania region database

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Introduction

Subjects with chronic disorders are more likely to be non-adherent and/or non-persistent to treatment than those with other diseases. Adherence is the extent to which patients take medication as prescribed by their physicians, whereas persistence is the time from treatment initiation to discontinuation.[1]
Low persistence rates to prescribed treatments induce an increased risk of fragility fractures. [2,3] The most common reasons for discontinuation from anti-osteoporotic medication were: side effects, costs, inconvenient dosing, advice from other specialists, socioeconomic conditions, and lack of motivation.[4]
The aim of our study is to analyze the rates and reasons for discontinuation of anti-osteoporotic drugs in the Campania Region.
We declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research project.

Table 1. Baseline characteristics of the study population

	Daily BP (n= 134)	Weekly BP (n= 15,354)	Monthly BP (n= 5,273)	Raloxifene (n= 198)	Strontium Ranelate (n= 9,089)	Total (n= 30,048)
Sex (female) n (%)	117 (87.31)	14,319 (93.26%)	5,000 (94.82%)	194 (97.98%)	8,687 (95.58%)	28,317 (94.24%)
Age (mean ± SD)	69.73 ± 10.16	69.16 ± 10.01	68.28 ± 10.07	63.58 ± 9.81	69.37 ± 9.89	69.04 ± 10.00
Switchers n (%)	29 (21.64%)	639 (4.16%)	359 (6.81%)	8 (4.04%)	497 (5.47%)	1,532 (5.1%)
Calcium and Vitamin D n (%)	48 (35.82%)	6,115 (39.83%)	3,217 (61.01%)	65 (32.83%)	4,264 (46.91%)	13,709 (46.62%)

* BP = Bisphosfonate

Table 2. Persistence over time with oral osteoporosis treatments (switching allowed)

	Total cohort (N=30,048)		Women (n=28,317)		Men (n=1,731)	
Time Point	Patients on therapy (%)	95% CI	Patients on therapy (%)	95% CI	Patients on therapy (%)	95% CI
3 months	59.2	58.6 - 59.8	59.4	58.8 - 60.0	55.5	53.1 - 57.8
6 months	34.8	34.2 - 35.4	35.1	34.5 - 35.7	31.1	29.0 - 33.3
9 months	22.3	21.9 - 22.7	22.5	22.1 - 22.9	18.5	16.8 - 20.3
1 year	13.4	13.0 - 13.8	13.5	13.1 - 13.9	10.9	9.6 - 12.3

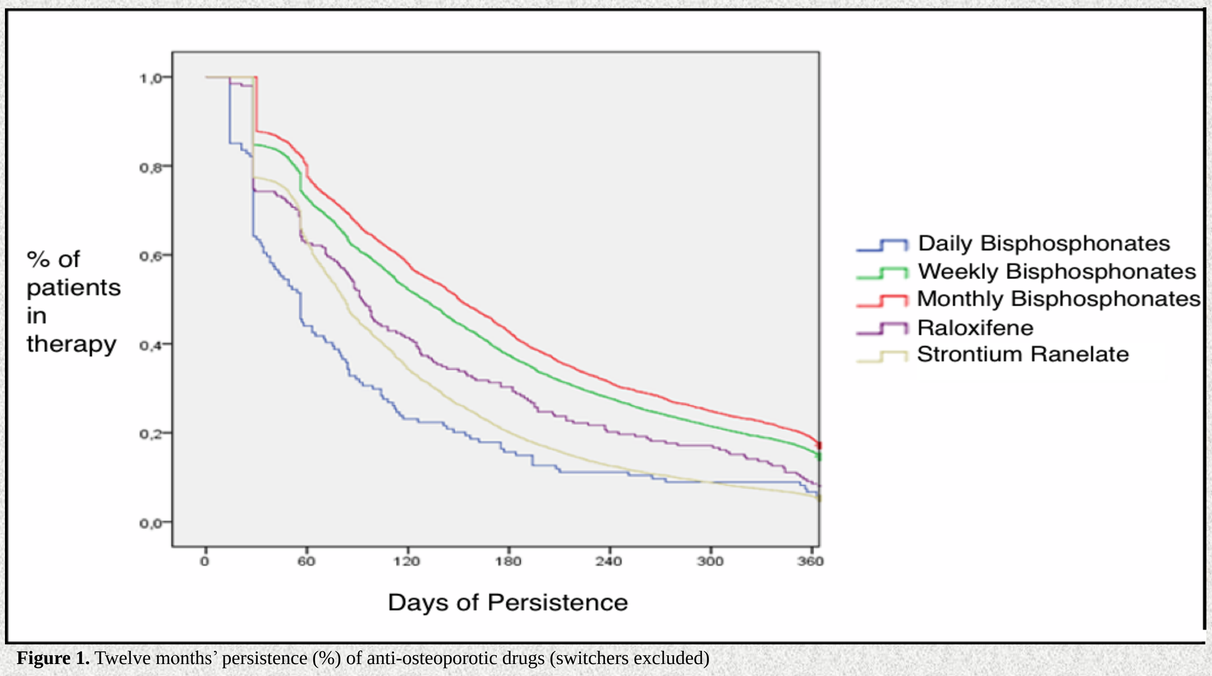

Figure 1. Twelve months' persistence (%) of anti-osteoporotic drugs (switchers excluded)

Methods

Subjects aged over 40 years were included if they receive at least one prescription for any anti-osteoporotic drugs for the first time (incident users) from 1st of July 2009 to 30th June 2010. The date of first prescription was considered as the index date. Data were obtained from an administrative database containing informations about outpatient drug prescriptions (i.e. drug code, dose, formulation, number of packages, date of prescription, and date of dispensation) dispensed in pharmacies in Campania Region. The drugs are classified according to the anatomical therapeutic chemical (ATC) classification system. Exclusion criteria were: patients who had been prescribed at least one anti-osteoporotic drug within one year before the index date; patients who did not reach at least 1 year of follow-up; patients who received only one prescription of anti-osteoporotic drug during the follow-up; patients who received a co-prescription of two different anti-osteoporotic drugs on the index date; subjects receiving anti-neoplastic drugs during follow-up. Patients were followed until the discontinuation of anti-osteoporotic therapy or until the end of the observation period (30th June 2011).
Patients were divided in continuers (subjects continuing the first-line anti-osteoporotic drug for at least 1 year), switchers (patients changing from the first-line to another medication) and discontinuers (patients interrupting the first-line drug during follow-up).
Persistence was evaluated determining the period during which no drug was available to the subject (gap method) according to the type of anti-osteoporotic drug. Discontinuation was defined if the gap between two prescriptions exceeded a period covered by drug prescribed > 1 month.
Persistence assessment derived from non-parametric survival analysis. Kaplan–Meier survival functions were estimated with treatment discontinuation as failure event. Statistical analyses were performed using SPSS software version 17.1 for Windows (SPSS Inc, Chicago, IL, USA).

Results

A total of 30,048 were incident users of anti-osteoporotic drugs: 1,731 (5.8%) males and 28,317 (94.2%) females. Baseline characteristics of the study population are shown in table 1. Weekly bisphosphonate (BP) (51.1%), was the most commonly prescribed drug, followed by strontium ranelate (30.2%), monthly bisphosphonate (17.5%), raloxifene (0.7%) and daily bisphosphonate (0.4%).
Co-prescription with calcium and vitamin D was most common for monthly bisphosphonate (61%). On the other hand, patients starting with daily bisphosphonate and weekly bisphosphonate were given fewer co-prescriptions of calcium and vitamin D (35.8% and 39.8%) respectively. In the overall study cohort, 1,532 (5.1%) were switchers. Switching rates were highest for patients taking daily bisphosphonate (21.6%) and lower for patients taking monthly bisphosphonate and weekly bisphosphonate (6.8% and 4%) respectively. In the overall cohort study, persistence rates were evaluated at 90, 180, 270 and 365 days after initiation of treatment. In the overall population, 34.8% of subjects were still on therapy after 6 months. At one year, persistent patients were 13.4%. Kaplan-Meier analysis showed the details grouped by individual regimen (figure 1). At 12 months the number of patients that remained on treatment were: monthly bisphosphonate 17.2%; weekly bisphosphonate 14.7%; raloxifene 8.1%; strontium ranelate 5.4%; daily bisphosphonate 5.2% log-rank test (2 degrees of freedom p <0.0001).(table 2)
A multivariate Cox proportional hazard analysis was estimated to identify variables that were significantly associated with non-persistence.(table 3) Patients who were initiated on daily regimen (HR 1.98) and strontium ranelate (HR 1.6) remained at a higher risk of early discontinuation compared to patients initiated with weekly regimen. Male gender was associated with a 11% higher risk of discontinuation. Patients who starting treatment with a co-prescription with calcium and vitamin D had a lower risk of early discontinuation.

Table 3. Determinants of non-persistence (multivariate Cox hazard model)

COVARIATES	HR	95% CI	
SEX			
Female	0.890	0.844	0.937
AGE (years)	1.000	0.999	1.002
DOSING REGIMEN*			
Daily BP** dosing regimen	1.983	1.626	2.420
Montly BP dosing regimen	0.929	0.896	0.963
Strontium Ranelate	1.614	1.568	1.660
Raloxifene	1.289	1.110	1.497
DRUG SWITCHING			
yes	0.673	0.599	0.756
CALCIUM + VITAMIN D SUPPLEMENTATION			
yes	0.717	0.699	0.736

* Weekly BP is the reference dosing regimen
** BP = Bisphosfonate

Conclusions

In clinical practice, anti-fracture effectiveness is significantly reduced by the high rate of discontinuation.[5] In our cohort, the persistence to different anti-osteoporotic treatments were significantly lower than reported in literature.[2] The most important determinants of both persistence and adherence to treatment are the type of drug and the dose regimen, with the worse persistence in subjects treated with daily BP or strontium ranelate. Switching rates were highest for patients taking daily BP or strontium ranelate and lower for patients taking weekly BP. The integration of strategies to enhance persistence to anti-osteoporotic drugs may have a widespread and economically sustainable impact and could improve treatment effectiveness and clinical outcomes in a real-life scenario.

References

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