POSTER: 782

Comparison of Two Doses of Zoledronic Acid for the Treatment of Osteoporosis in HIV Infected Patients. Results of a Randomized Open Label Study (VIHZOL Study).

Eugènia Negredo[1], Anna Bonjoch[1], Núria Pérez-Álvarez[1,2], Arelly Ornelas[1,3], Jordi Puig[1], Cristina Herrero [1] , Patricia Echeverría[1], Bonaventura Clotet[1,4].

[1] Lluita contra la Sida Foundation, Germans Trias i Pujol University Hospital, Badalona, Spain. Universitat Autònoma de Barcelona, Spain.[2] Statistics and Operations Research Department, Universitat Politècnica de Catalunya, Barcelona, Spain. [3] Department of Econometrics, University of Barcelona, Barcelona, Spain. [4] Irsicaixa Foundation, Germans Trias i Pujol University Hospital, Badalona, Spain.

Address for correspondence: Eugenia Negredo, MD, PhD
enegredo@flsida.org

BACKGROUND

An increasing proportion of patients require specific therapy for osteoporosis. Bisphosphonates are currently considered the most appropriate treatment for osteoporosis in generla population.

Studies in HIV-infected patients support the efficacy and safety of alendronate and, more recently, zoledronate. Given the need for easily managed low-toxicity treatment of osteoporosis in HIV-infected patients, the present study evaluates the efficacy and tolerability of the latest bisphosphonate, zoledronate, by comparing annual and biennial administration.

DESIGN and OBJECTIVES

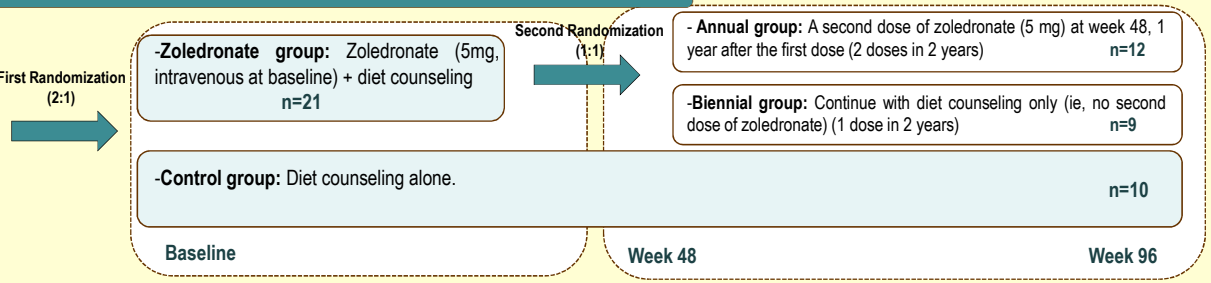
Design: A 96-week, controlled, and randomized pilot in HIV-infected patients with osteoporosis.
The study was approved by the Institutional Ethics Committee of the coordinating center and the local health authorities (NCT 00795483).
Principal objective: to compare the efficacy of zoledronate administered biennially with that of zoledronate administered annually and with a control group. The percentage of changes in BMD and T-scores were recorded at week 96. In order to assess the durability of the effect of zoledronate, changes in BMD and T-scores were also compared in each group at weeks 48 and 96.
Secondary objectives: to measure changes in BMD at week 48 between the zoledronate group and the control group. We also compared changes in markers of bone formation and resorption between groups at week 96 and within groups at weeks 48 and 96. Safety and tolerability of zoledronate were also assessed.

STUDY PATIENTS AND RANDOMIZATION

Inclusion criteria: Patients with chronic HIV-1 infection and low bone mineral density (BMD) by dual-energy x-ray absorptiometry (DXA) (WHO classification: T-score <–1.0 SD in the lumbar spine or hip).

Exclusion criteria hypocalcemia, increased creatinine levels (>2.3 mg/mL), glomerular filtration rate <60 mL/min/1.73m^2 (estimated using the Modification of Diet in Renal Disease equation), causes of secondary osteoporosis other than hypovitaminosis D, and treatment for osteoporosis during the previous 4 months.

All the patients who agreed to participate in the study gave their signed informed consent.



RESULTS

Table 1. Baseline characteristics of patients

	Control group (n=10)	Annual group (n=12)	Biennial group (n=9)	P value
Age, years	48.6 (41.6;58.8)	49.4 (45.6;57)	46.4 (44.35;58.3)	0.966
Gender, male (%)	90	91	78	0.609
Route (%)				0.625
MSM	50	58	34	
Intravenous drug user	30	25	22	
Heterosexual	20	8	44	
Unknown	-	9	-	
Time since diagnosis of HIV infection (months)	186.5 (146.75;213)	119 (78.75;222.25)	191 (124;249)	0.459
Baseline antiretroviral therapy (%)	60	58	44	0.756
Protease inhibitor	50	42	33	0.763
NNRTI				
Time on antiretroviral therapy (months)	171 (141.75;207.75)	116.5 (64.5;177.75)	138 (122.5;212)	0.360
Nadir CD4 (cells/mm^3)	271.5 (130.75;383)	179.5 (75.5;248.5)	222 (34.5;298.5)	0.263
CD4 (cells/mm^3)	574 (342.25;848)	493.5 (332;570.25)	600(529;783)	0.284
Body mass index (kg/m^2)	25.72 (21.5;26.68)	23 (19.97;25.42)	24.16 (20.21;24.98)	0.259

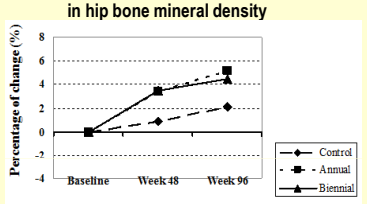
Data are expressed as median and interquartile range unless otherwise indicated. MSM, men who have sex with men; NNRTI, Non-nucleotide reverse transcriptase inhibitor.

Table 2. Changes in L1-L4 and femoral bone mineral density and T-scores

	Control group (n=10)	Annual group (n=12)	Biennial group (n=9)	P value		
Osteoporosis (%)						
Baseline	70	66.7	66.7	0.983		
Wk 48	75	33	22	0.067		
Wk 96	43	18	22	0.484		
	Control group (n=10)	Annual group (n=12)	Biennial group (n=9)	P value control-annual	P value control-biennial	P value annual-biennial
L1-L4 BMD						
Baseline	1.01 (0.95;1.1)	0.94 (0.89;1.06)	0.93 (0.92;1.02)	0.391	0.221	0.972
Wk 48	0.98 (0.91;1.1)	0.99 (0.95;1.1)	0.99 (0.96;1.07)	0.396	0.564	0.915
Wk 96	1.01 (0.95;1.09)	1.04 (0.96;1.1)	0.98 (0.96;1.06)	0.221	0.791	0.254
L1-L4 T-score						
Baseline	−1.85 (−2.3 ;−1.17)	−2.5 (−2.8;−1.47)	−2.3 (−2.6;−1.75)	0.261	0.175	0.858
Wk 48	−2.1 (−2.7;−1.07)	−2.05 (−2.6;1.1)*	−2 (−2.2;−1.45) *	0.279	0.531	1
Wk 96	−1.8 (−2.4;−1.2)	−1.6 (−2.3;−1) *	−1.9 (−2.2;−1.5) *	0.236	0.710	0.563
Total femur BMD						
Baseline	0.84 (0.82;0.88)	0.80 (0.78;0.89)	0.82 (0.74;0.87)	0.489	0.205	0.670
Wk 48	0.84 (0.8;0.90)	0.83 (0.81;0.91)	0.85 (0.78;0.87)	0.877	0.923	0.831
Wk 96	0.84 (0.83;0.9)	0.84 (0.82;0.95)	0.84 (0.76;0.89)	0.964	0.672	0.518
Total femur T-score						
Baseline	−1.9 (−2.1;−1.5)	−1.9 (−2.3 ;−1.5)	−2.1 (−2.4;−1.7)	0.529	0.203	0.748
Wk 48	−1.85 (−2.2;−1.2)	−1.75 (−2;−1.32) *	−1.8 (−2.15;−1.6) *	0.847	0.885	0.643
Wk 96	−1.9 (−1.9;−1.4)	−1.8 (−2.1;−1.1) *	−1.9 (−2.2;−1.5) *	0.791	0.758	0.381

Data are expressed as median and interquartile range unless otherwise indicated. *p<0.05 when compared with baseline in the within-group analyses.

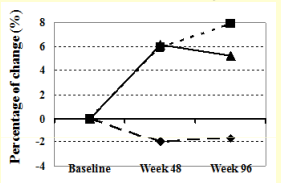
Figure 1A. Median of the percentage of change in hip bone mineral density



At week 48, p=0.045 between control and zoledronate groups.

At week 96, p=0.042 between control and annual groups; p=0.342 between annual and biennial groups.

Figure 1B. Median of percentage of change in L1-L4 bone mineral density.

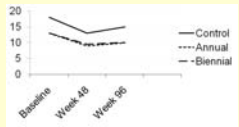


At week 48, p=0.002 between control and zoledronate groups.

At week 96, p=0.003 between control and annual groups; p=0.017 between control and biennial groups and p=0.184 between annual and biennial groups.

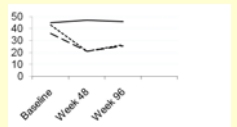
Figure 2. Changes in bone markers

Serum alkaline phosphatase (µgr/L)



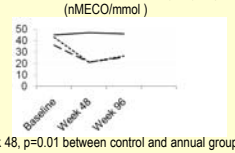
At week 96, p=0.004 between control and annual groups; p=0.012 between control and biennial groups; and p=0.972 between biennial and annual groups.

Serum procollagen type 1 amino-terminal propeptide (P1NP) (ng/mL)



At week 48, p=0.001 between control and annual groups; p=0.015 between control and biennial groups.

Urine N-telopeptide of type 1 collagen (NTx) (nMECO/mmol)



At week 48, p=0.01 between control and annual groups; p=0.015, between control and biennal groups.

At week 96, p=0.013 between control and annual groups; p=0.083 between control and biennal groups.

Security: Two patients from the control group were lost to follow-up. After the first infusion of zoledronate, 2 patients had grade 1 asthenia and 2 had fever (grade 1 and grade 2); these symptoms resolved within 48 hours.
Two patients from the control group and 4 from the zoledronate group received calcium supplements to achieve a daily intake of 1,200 mg.

CONCLUSIONS

The use of biennial zoledronic acid presented similar bone benefit than the annual administration after 96 weeks of follow up in terms of BMD and bone markers.

The biennial administration of zoledronic acid may be an alternative in the treatment of osteoporosis in this population to prevent toxicity and reduce costs.