Calcif Tissue Int (2001) 69:242–247
DOI: 10.1007/s00223-001-1060-8

Calcified Tissue International

Risedronate Increases Bone Density and Reduces Vertebral Fracture Risk Within One Year in Men on Corticosteroid Therapy

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Received: 2 May 2001 / Accepted: 11 May 2001 / Online publication: 27 September 2001

Abstract. Limited information is available on the effect of bisphosphonates in men receiving corticosteroid therapy. We studied 184 men among the patients enrolled in two, double-blind, placebo-controlled, 1-year studies with similar protocols. The studies evaluated the effects of risedronate in patients beginning corticosteroid treatment at a dose of at least 7.5 mg per day of prednisone or equivalent (prevention study) or continuing long-term treatment of corticosteroid at that dose (treatment study). The men received either placebo or risedronate (2.5 mg or 5 mg) daily, along with calcium supplementation (500–1000 mg). Endpoints included differences in bone mineral density (BMD) at the lumbar spine, femoral neck, and femoral trochanter, assessment of vertebral fractures, changes in biochemical markers of bone turnover, and overall safety. In the treatment study, risedronate 5 mg significantly ($P < 0.01$) increased lumbar spine BMD by 4.8% at the lumbar spine, 2.1% at the femoral neck, and 2.6% at the femoral trochanter compared with baseline values. In the prevention study, bone loss was prevented with risedronate 5 mg; in the placebo group, BMD decreased significantly ($P < 0.01$) by 3.4%, 3.3%, and 3.4% in the lumbar spine, femoral neck, and trochanter, respectively, at 1 year. The differences between risedronate 5 mg and placebo groups were significant at all skeletal sites in the prevention study ($P < 0.01$) and at the lumbar spine in the treatment study ($P < 0.001$). The 2.5 mg dose also had a positive effect on BMD, although of a lesser magnitude than the 5 mg dose. When the data from the two studies were combined, the incidence of vertebral fractures decreased 82.4% (95% confidence interval, 36.6%–95.1%) in the pooled risedronate groups compared with placebo ($P = 0.008$). Risedronate was well tolerated in men, with a similar incidence of upper gastrointestinal adverse events in the placebo and treatment groups. Daily treatment with risedronate increases bone density and decreases vertebral fracture risk within 1 year in men receiving corticosteroid therapy.

Key words: Risedronate — Corticosteroid therapy — Vertebral fracture risk, men

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Long considered a disease of postmenopausal women, osteoporosis is increasingly being recognized among the growing population of elderly men. The annual number of hip fractures in men is expected to exceed 1.1 million by 2025 [1]. Although one of the most common causes of secondary osteoporosis in men is corticosteroid treatment, limited data are available concerning the prevention and treatment of corticosteroid-induced osteoporosis (CIO) in men.

Risedronate, a novel pyridinyl bisphosphonate, is effective in the treatment and prevention of postmenopausal osteoporosis in women and corticosteroid-induced osteoporosis in men and women (CIO) [2–8]. In postmenopausal osteoporosis trials, risedronate has been shown to reduce the risk of vertebral fractures in the first year of treatment and the risk of hip fractures over 3 years [2–4]. Risedronate also reduced the risk of vertebral fracture by 70% in a mixed population of men and women initiating or continuing corticosteroid treatment for chronic conditions [8]. Because data on the efficacy of bisphosphonates in the management of osteoporosis in men are limited, we evaluated the efficacy and safety of risedronate in the male patients receiving corticosteroids that were enrolled in two double-blind, placebo-controlled studies conducted in parallel under similar protocols [5, 6].

Methods

Patients and Treatments

A total of 184 ambulatory men, 18–85 years of age and receiving at least 7.5 mg oral prednisone daily or equivalent oral corticosteroid therapy, were enrolled in two parallel studies and received at least one dose of study drug. Men were expected to continue on corticosteroid therapy for at least 12 months. One study included 77 men who had been treated with corticosteroids for 3 months or less (prevention study) [5]. The second study included 107 men who had received corticosteroid therapy for at least 6 months (treatment study) [6]. The underlying diseases requiring corticosteroid treatment included rheumatoid arthritis, lung disease, polymyositis, polymyalgia rheumatica, temporal arteritis, and vasculitis. The exclusion criteria included evidence of metabolic bone disease other than CIO, recent use of drugs known to affect bone

metabolism, and any significant organic or psychiatric disease that could affect participation or interfere with the interpretation of the data. Patients with a history of or an on-going upper gastrointestinal disorder or use of nonsteroidal antiinflammatory drugs (NSAIDs) or aspirin were not excluded. The protocol was approved by the respective ethics committees or institutional review boards, and all patients gave written informed consent.

The men received either placebo (60 patients), risedronate 2.5 mg (61 patients), or risedronate 5 mg (63 patients) daily for 1 year. In the prevention study, all patients received 500 mg elemental calcium daily. All patients in the treatment study received 1000 mg elemental calcium and 400 IU vitamin D daily.

Measurements

Bone densitometry measurements were performed at baseline and after 1 year by dual-energy X-ray absorptiometry (DXA), using either Lunar (Madison, Wisconsin, U.S.A) or Hologic (Waltham, Massachusetts, USA) instruments. Lumbar spine BMD values were standardized to adjust for machine type [9]. All results were analyzed centrally by the Osteoporosis and Arthritis Research Group at the University of California at San Francisco, USA. Dual-energy X-ray absorptiometry phantom data were analyzed for consistency of instrument performance throughout the study [10]. Longitudinal BMD correction factors were applied to compensate for instrument variations, if necessary.

Lateral radiographs of the thoracic and lumbar spine (T4–L4) were taken at baseline and at 12 months, and evaluated at a central facility for prevalence and incidence of vertebral fractures. The assessment of vertebral fractures was made using quantitative morphometry, in accordance with the recommendations of the Working Group on Vertebral Fractures [11]. A vertebra was considered to be fractured at baseline (prevalent fracture) if any of the vertebral height ratios fell below three standard deviations of the mean for the study population, as described by Melton et al. [12]. A new (incident) vertebral fracture was defined as a decrease of $\geq$15% (for intact vertebrae at baseline) or a decrease of $\geq$4 mm (for fractured vertebrae at baseline) in any of the measured vertebral heights (anterior, middle, or posterior). In addition, all incident vertebral fractures identified by morphometry were verified visually by a skeletal radiologist (Massachusetts General Hospital, Boston, MA).

Measurements of biochemical markers of bone formation [serum bone-specific alkaline phosphatase (BAP)] and bone resorption [urinary N-telopeptide (NTx), adjusted for creatinine excretion] were performed at baseline and 1, 3, 6, and 12 months, using the Tandem-R Ostase immunoradiometric assay (Hybritech, Inc., San Diego, California, USA) and an enzyme-linked immunosorbent assay (Ostex International, Seattle, Washington, USA), respectively. The intra-and interassay coefficients of variation were 6.8% and 7.5%, respectively, for BAP, and 7.3% and 12.2%, respectively, for NTx. Samples were analyzed by the Nichols Institute at Quest Diagnostics, San Juan Capistrano, California, USA.

Adverse events were recorded at all post baseline visits, and their severity and relationship to study drug were evaluated by the investigators.

Statistical Analysis

Results reported here are based on an intent-to-treat (ITT) population, defined as randomized male patients who took at least 1 dose of study drug. The pooled analysis was possible because of the similarity of the study designs and underlying diseases in the prevention and treatment studies. The two study populations differed in the duration of corticosteroid therapy prior to enrollment (3 months or less versus 6 months or more), and in the amount of vitamin D and calcium supplementation. The statistical methodology accounted for trial differences, and a stratified (by trial) analysis was conducted, which averaged the treatment effect in the two studies.

All statistical analyses were conducted at the 5% significance level, two-sided. Within-treatment group comparisons were carried out using the one-sample, paired *t*-test. A two-way ANOVA model (with trial and treatment as factors) was used for comparisons between treatment groups. A comparison of the incidence of vertebral fractures between the combined risedronate (2.5 mg and 5 mg) and placebo groups was performed using the Cochran-Mantel-Haenszel test, with trial as a stratification factor. Data are shown as mean and standard error (SE) unless otherwise specified.

Results

A total of 184 male patients received at least one dose of study drug (ITT population). The baseline characteristics of the 184 enrolled patients were similar between treatment groups (Table 1). At baseline, the mean lumbar spine BMD was similar in the risedronate and placebo groups. The mean daily corticosteroid dose prior to enrollment was 19.4 mg (SD, 16.4) and the mean corticosteroid dose during the 1-year study was 14.2 mg (SD, 15.7); the corticosteroid doses were similar among the three treatment groups. Forty percent of men had prevalent (baseline) vertebral fractures; the prevalence was slightly higher in the risedronate 5 mg group (46%) than in the other groups (Table 1).

Bone Mineral Density

At 1 year, a significant difference between the risedronate 5 mg and placebo groups in mean percent change from baseline in BMD was noted at all skeletal sites in the treatment study. The mean differences (SE) versus baseline at 1 year in the risedronate 5 mg group were 4.8% (0.8), 2.1% (0.7), and 2.6% (0.5) at the lumbar spine, femoral neck, and femoral trochanter, respectively ($P < 0.01$) (Fig. 1a). At 1 year, the difference between the risedronate 5 mg and placebo groups was significant at the lumbar spine ($P < 0.001$) but not at the femoral neck or femoral trochanter. In the prevention study, significant losses of 3.4% (0.8), 3.3% (1.1), and 3.4% (0.9) were observed at the lumbar spine, femoral neck, and femoral trochanter, respectively, in the placebo group ($P < 0.01$) whereas BMD was maintained in the risedronate 5 mg group (Fig. 1b). The difference between the risedronate 5 mg and placebo groups was significant at all sites ($P < 0.01$). The risedronate 2.5 mg dose produced smaller changes in BMD than the 5 mg dose in both the prevention and treatment studies (Fig. 1).

Vertebral Fractures

In the placebo group, 9 of 38 (24%) patients sustained a vertebral fracture compared with 0 of 25 in the risedronate 2.5 mg group and 3 of 33 (9%) in the risedronate 5 mg group. The distribution of patients with vertebral fractures was similar between the two studies: 5 patients in the prevention study (4 placebo and 1 risedronate 5 mg) and 7 patients (5 placebo and 2 risedronate 5 mg) in the treatment study. The number of vertebral fractures was 18 in the placebo group and 3 in the risedronate 5 mg group, indicating

Table 1. Baseline characteristics of the study population

	Placebo	2.5 MG Risedronate	5 MG Risedronate
Characteristic			
Total enrolled (N)	60	61	63
Prevention study	25	25	27
Treatment study	35	36	36
Age (years) - mean (SD)	54.9 (13.07)	59.2 (12.94)	58.8 (13.30)
Underlying disease - n (%)			
Rheumatoid arthritis	25 (41.0)	21 (33.9)	25 (39.7)
Lung disease	14 (23.0)	12 (19.4)	15 (23.8)
Polymyositis	3 (4.9)	2 (3.2)	2 (3.2)
Polymyalgia rheumatica	4 (6.6)	10 (16.1)	10 (15.9)
Temporal arteritis	4 (6.6)	5 (8.1)	2 (3.2)
Vasculitis	5 (8.2)	3 (4.8)	3 (4.8)
Duration of prior corticosteroid therapy - n (%)			
≤3 months	24 (40.0)	25 (41.0)	24 (38.1)
3–6 months	1 (1.7)	2 (3.3)	4 (6.4)
>6 months	35 (58.3)	34 (55.7)	35 (55.5)
Lumbar spine bone mineral density (standardized) - mg/cm^2 mean (SE)			
Prevention study	1123 (36.5)	1097 (45.9)	1194 (36.2)
Treatment study	984 (27.7)	1002 (19.7)	959 (30.5)
T-score for the lumbar spine - mean (SE)			
Prevention study	−0.47 (0.34)	−0.89 (0.40)	0.15 (0.30)
Treatment study	−1.67 (0.29)	−1.42 (0.20)	−1.89 (0.30)
Prevalent vertebral fractures - n (%)	22 (36.7)	23 (38.3)	29 (46.8)
Biochemical markers of bone turnover - mean			
Urinary N-telopeptide (nmol BCE/mmol creatinine)	59.2 (5.7)	65.0 (8.6)	53.3 (3.9)
Serum bone-specific alkaline phosphatase (μg/l)	10.8 (0.61)	10.3 (0.62)	10.7 (0.53)

that placebo men had more multiple fractures than risedronate-treated patients. When the risedronate groups were combined for analysis, risedronate treatment produced a significant reduction of 82.4% (95% confidence interval, 36.6%–95.1%, $P = 0.008$) in vertebral fracture risk compared with placebo (Fig. 2).

Bone Turnover Markers

At baseline, the mean values for urinary NTx and serum BAP were similar in all treatment groups. A median decrease in urinary NTx of 54.0% ($P < 0.001$) was observed in the risedronate 5 mg group after the first month of treatment. At 1 year, the median decrease was 61.0% ($P < 0.001$) compared with baseline. Corresponding decreases in the risedronate 2.5 mg and placebo groups at 1 year were 46.5% ($P < 0.001$) and −17.1% (not significant), respectively. Median decreases in serum levels of BAP were evident within the first month of treatment in the risedronate 5 mg group and were sustained throughout the 1-year study. At 1 year, decreases in the risedronate 5 mg, risedronate 2.5 mg, and placebo groups were 20.2% ($P < 0.01$), 4.0% (not significant), and 11.0% ($P = 0.005$), respectively.

At 1 year, the between-group difference for the placebo and risedronate 5 mg groups was −48.6% ($P < 0.001$) for urinary NTx and −33.1% ($P < 0.001$) for serum levels of BAP.

Adverse Events

The incidence of serious adverse events and those leading to withdrawal was similar in the risedronate and placebo groups (Table 2). Upper gastrointestinal adverse events also occurred at a similar incidence in all treatment groups. The most common upper gastrointestinal adverse events were abdominal pain, nausea, and diarrhea. There were no clinically relevant changes in laboratory parameters including hematology, liver, and kidney function tests.

Discussion

This study demonstrates that risedronate is effective and well tolerated in the prevention and treatment of CIO in men. After 1 year of treatment, risedronate significantly increased BMD at the lumbar spine, femoral neck, and femoral trochanter compared with baseline in men who had been on at least 7.5 mg oral prednisone daily or the equivalent for at least 6 months. In the prevention study, signifi-

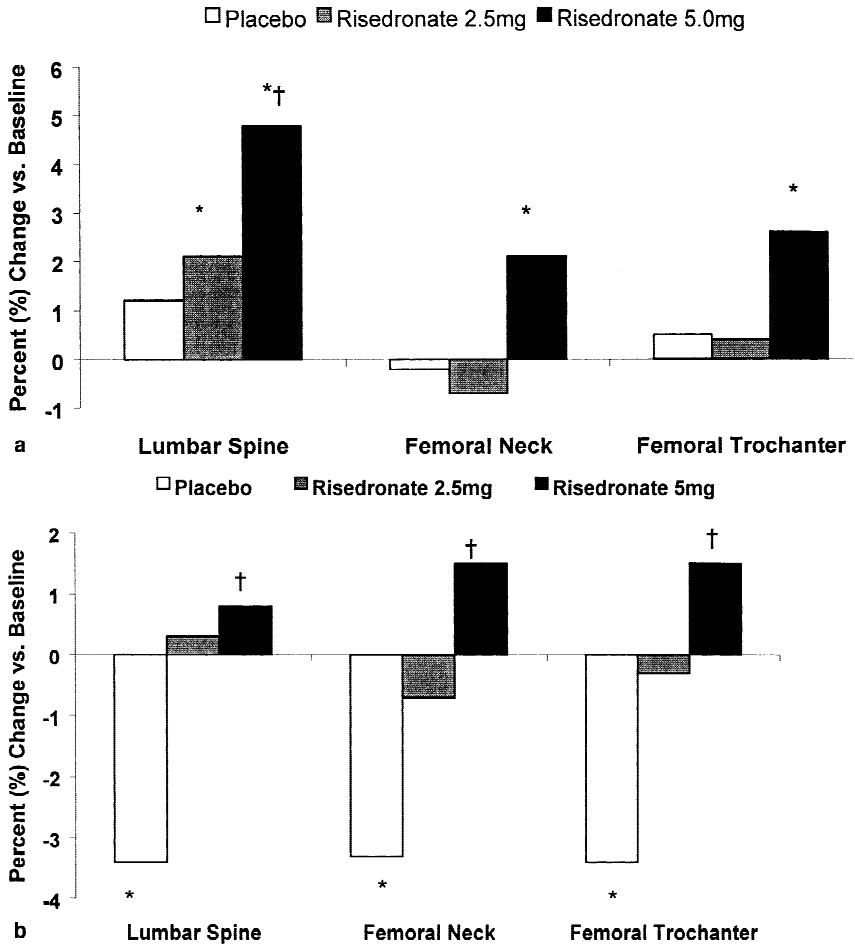

Fig. 1. (**a**). Effect of risedronate on BMD of the lumbar spine, femoral neck, and femoral trochanter in men receiving 7.5 mg or more of oral prednisone daily or equivalent for 6 months or longer (treatment study). (**b**) Effect of risedronate on BMD of the lumbar spine, femoral neck, and femoral trochanter in men receiving 7.5 mg or more of oral prednisone daily or equivalent for 3 months or less (prevention study). *Significant difference versus baseline, $P < 0.01$; † difference versus control, $P<0.01$.

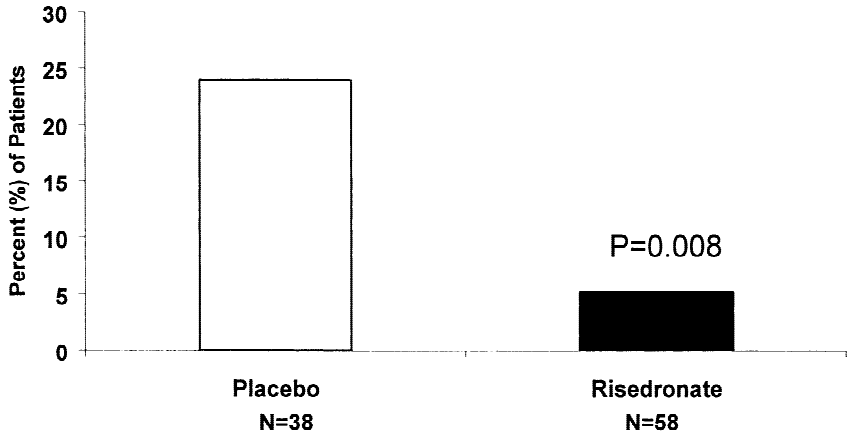

Fig. 2. Incidence of vertebral fractures in patients receiving placebo and risedronate 2.5 mg and 5 mg daily for 1 year.

cant decreases in BMD were observed at all sites in the placebo patients, despite calcium supplementation, demonstrating that men on corticosteroids lose substantial bone mass during the first year of corticosteroid treatment. In the risedronate group, BMD was maintained at all sites.

Men in the risedronate group experienced a significant 82% reduction in vertebral fractures within 1 year compared with men in the placebo group ($P = 0.008$). Importantly, 24% of the men in the placebo group sustained a vertebral fracture during the year, demonstrating that men are at a substantial risk for fracture during corticosteroid treatment, which is similar or somewhat higher than that observed in postmenopausal women receiving corticosteroid therapy [8, 13, 14]. In addition, 40–46% of the men had a baseline prevalent vertebral fracture despite a mean baseline BMD T-score which would not have been in the osteoporotic

Table 2. Summary of selected adverse events

Adverse event (AE)	Placebo (n = 60)	2.5 mg Risedronate (n = 61)	5 mg Risedronate (n = 63)
Patients with AEs	58 (96.7)	55 (90.2)	59 (93.7)
Patients with drug-related AEs[a]	20 (33.3)	16 (26.2)	17 (27.0)
Patients with upper GI AEs	13 (21.7)	6 (9.8)	11 (17.5)
All upper gastrointestinal AEs			
Abdominal pain	6 (10)	1 (1.6)	5 (7.9)
Nausea	3 (5)	4 (6.6)	4 (6.3)
Diarrhea	6 (10)	3 (4.9)	5 (7.9)
Esophagitis	1 (1.7)	0 (0)	0 (0)
Duodenitis, gastritis	0 (0)	1 (1.6)	1 (1.6)
Esophageal ulcer	0 (0)	1 (1.6)	0 (0)
Moderate-to-severe upper gastrointestinal AEs	6 (10.0)	1 (1.6)	3 (4.8)

Values are number (%) of patients
[a]Those events with a possible or probable relationship to the study drug as assessed by the investigator.

range for women, suggesting that men receiving corticosteroids sustain fractures at higher BMD levels. The 82% reduction in vertebral fracture risk in men that we report is consistent with the 1-year fracture vertebral reductions observed with risedronate in the postmenopausal women receiving corticosteroids (73% reduction) [8] and in women with postmenopausal osteoporosis (61–65% reduction in 1 year) [3, 4].

There are limited treatment data available in males with primary or corticosteroid-induced osteoporosis. Saag et al. [14] recently reported that alendronate increased BMD at the lumbar spine compared with baseline values, but did not significantly reduce the incidence of vertebral fractures in the first year of treatment in men receiving corticosteroids, although the number of men with vertebral fractures was small. The latter study was extended up to 2 years but was unable to examine the effect of alendronate on vertebral fractures in men since, suprisingly, no fractures were observed in either placebo or alendronate arms [15].

There are some limitations to our report. Our analysis was conducted on a subgroup of men from two CIO studies combining two doses of risedronate. However, the two studies had similar protocols and both doses of risedronate had a favorable effect on BMD relative to placebo. In both studies risedronate-treated men had fewer vertebral fractures compared with men in the placebo group, supporting the consistency of risedronate's therapeutic effect. Another limitation is that the effect of risedronate beyond 1 year was not studied in men on corticosteroid therapy, and therefore the treatment duration for a long-term prevention of fractures remains to be determined.

In conclusion, treatment with risedronate prevents bone loss or increases bone mass in men initiating or continuing long-term corticosteroid therapy. Approximately 24% of the placebo patients experienced a vertebral fracture, indicating that these men are at substantial risk for vertebral fractures during 1 year. Risedronate significantly reduced this risk of vertebral fractures. Risedronate is well tolerated in this compromised population of men receiving concomitant corticosteroid therapy.

Acknowledgments. This work was supported by a grant from Procter & Gamble Pharmaceuticals, Cincinnati, Ohio, and Aventis Pharma, Bridgewater, New Jersey.

Appendix

Other investigators participating in the Prevention and Treatment studies were: **Prevention Study:** Eugene Boling, Rancho Cucamonga, CA - Walter Briney, Denver, CO - J. Brown, Quebec, Canada - Selwyn A. Cohen, Trumbull, CT - Ronald D. Emkey, Reading, PA - Susan C. English, Billings, MT - Maria Greenwald, Palm Springs, CA - Thomas N. Hangartner, Dayton, OH - Hunter Heath, Salt Lake City, UT - Matthew Heller, Peabody, MA - Rebecca D. Jackson, Columbus, OH - Michael Keller, San Diego, CA - M. Maricic, Tucson, AZ - Robert M. Levy, Olympia, WA - Harris H. McIlwain, Tampa, FL - C. Rosen, Bangor, Maine - Sanford Roth, Phoenix, AZ - Marshall Sack, Austin, TX - Elliott Schwartz, Oakland, CA - Kathryn L. Sewell, Boston, MA - Daniel Small, Sarasota, FL - Stanley Wallach, New York, NY - John L. Stock, Worcester, MA - Kyle Strader, Raleigh, NC - Nathan Wei, Frederick, MD - Thomas M. Zizic, Baltimore, MD. **Treatment Study:** C. Benhamou, Orléans, France - B. Bresnihan, Dublin, Eire - A. Crisp, Cambridge, U.K. - J. Davies, Bath, U.K. - B. Devulder, Lille, France - S.M. Doherty, Hull, U.K. - A. Fairney, London, U.K. - P. Godard, Montpellier, France - G. Huchon, Boulogne, France - David J. Hosking, Nottingham U.K. - R.A. Hughes, Chertsey, U.K. - J.M. Kaufman, Gent, Belgium - R.F. Laan, Nijmegen, Netherlands - M. Molloy, Cork, Eire - P. Ryan, Gillingham, U.K. - T.D. Spector, London, U.K. - H. Taggart, Belfast, Northern Ireland - P. Thompson, Poole, U.K. - G. Weryha, Vandoeuvre, France - T. Wilkin, Plymouth, U.K. - A. Woolf, Truro, U.K.

References

1. Cooper C, Campion G, Melton LJ III (1992) Hip fractures in the elderly: a world-wide projection. Osteoporos Int 2:285–289
2. McClung MR, Geusens P, Miller PD, Zippel H, Bensen WG, Roux C, Adami S, Fogelman I, Diamond T, Eastell R, Meunier PJ, Reginster J-Y (2001) Effect of risedronate on hip fracture in elderly women. N Engl J Med 344:333–340
3. Reginster JY, Minne HW, Sorensen OH, Hooper M, Roux C, Brandi ML, Lund B, Ethgen D, Pack S, Roumagnac I, Eastell R (2000) Randomized trial of the effects of risedronate on vertebral fractures in women with established postmenopausal osteoporosis. Osteoporosis Int 11:83–89
4. Harris ST, Watts NB, Genant HK, McKeever CD, Hangartner T, Keller M, Chesnut CH, Brown J, Eriksen EF, Hoseyni MS, Axelrod DW, Miller PD (1999) Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized, controlled trial. JAMA 282:1344–1352
5. Cohen S, Levy RM, Keller M, Boling E, Emkey RD, Greenwald M, Zizic TM, Wallach S, Sewell KL, Lukert BP, Axelrod DW, Chines AA (1999) Risedronate therapy prevents corticosteroid-induced bone loss. Arthritis Rheum 42:2309–2318
6. Reid DM, Hughes RA, Laan R, Sacco-Gibson NA, Wenderoth DH, Adami S, Eusebio R, Devogelaer JP (2000) Efficacy and safety of daily risedronate in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. J Bone Miner Res 15:1006–1013
7. Eastell R, Devogelaer JP, Peel NFA, et al. Prevention of bone loss with risedronate in glucocorticoid-treated rheumatoid arthritis patients. Osteoporosis Int 4:331–337
8. Wallach S, Cohen S, Reid DM, Hughes RA, Hosking DJ, Laan RF, Doherty SM, Maricic M, Rosen C, Brown J, Barton I, Chines AA (2000) Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy. Calcif Tissue Int 67:277–285
9. Genant HK, Grampp S, Gluer CC, Faulkner KG, Jergas M, Engelke K, Hagiwara S, Van Kuijik C (1994) Universal standardization for dual X-ray absorptiometry: patient and phantom cross-calibration results. J Bone Miner Res 9:1503–1514
10. Faulkner KG, McClung MR (1995) Quality control of DXA instruments in multicenter trials. Osteoporosis Int 5:218–227
11. Kiel D (1995) Assessing vertebral fractures: National Osteoporosis Working Group on Vertebral Fractures. J Bone Miner Res 10:518–523
12. Melton LJ III, Lane AW, Eastell R, O'Fallon WM, Riggs BL (1993) Prevalence and incidence of vertebral deformities. Osteoporosis Int 3:113–119
13. Adachi JD, Bensen WG, Brown J, Hanley D, Hodsman A, Josse R, Kendler DL, Lentle B, Olszynski W, Ste-Marie LG, Tenenhouse A, Chines AA (1997) Intermittent etidronate therapy to prevent corticosteroid-induced osteoporosis. N Engl J Med 337:382–387
14. Saag KG, Emkey R, Schnitzer TJ, Brown JP, Hawkins F, Goemaere S, Thamsborg G, Liberman UA, Delmas PD, Malice MP, Czachur M, Daifotis AG (1998) Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. N Engl J Med 339:292–299
15. Adachi JD, Saag KG, Delmas PD, Liberman UA, Emkey RD, Seeman E, Lane NE, Kaufman J-M, Poubelle PEE, Hawkins F, Correa-Rotter R, Menkes C-J, et al. Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids. Arthritis Rheum 44:202–211