FPIN's Help Desk Answers

Duration of Bisphosphonate Therapy

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Clinical Question

What is the optimal duration of bisphosphonate therapy for the treatment of osteoporosis in postmenopausal women?

Evidence-Based Answer

Oral bisphosphonates significantly reduce clinical fracture risk at four years in women with postmenopausal osteoporosis (T-score less than –2.5). (Strength of Recommendation [SOR]: B, based on a randomized controlled trial [RCT] with subgroup analysis.) Treatment beyond five years is associated with further reductions in fractures in women with persistent femoral neck T-scores less than –2.5. (SOR: C, based on a post-hoc analysis of RCTs.) Treatment beyond five years in other women with osteopenia or osteoporosis does not result in further decreases in rates of clinical vertebral fractures, nonvertebral fractures, or mortality. (SOR: C, based on a meta-analysis of two small RCTs reporting fracture as a secondary outcome.)

Evidence Summary

A 2011 meta-analysis of three RCTs in postmenopausal women with primary osteoporosis (N = 1,443) evaluated continual oral bisphosphonate treatment vs. discontinuation at five years.[1] Study participants had a bone mineral density (BMD) of 0.68 g per cm^2 or less (corresponding to a T-score of –1.6) in one trial or a T-score of –2.5 or less in two trials, or a history of fracture. Oral bisphosphonates included alendronate (Fosamax), 5 or 10 mg per day, or etidronate (Didronel), 400 mg per day. Outcomes included change in BMD, rates of bone turnover, mortality, and adverse events. Fracture rates were reported but were not primary outcomes in any of the trials. Comparing a discontinuation group (patients who stopped bisphosphonate therapy after five years) with a continuation group (extended bisphosphonate treatment for seven to 10 years), pooled analysis of two of the trials (N = 1,346) showed no difference in the risk of vertebral fracture (relative risk [RR] = 0.61; 95% confidence interval [CI], 0.32 to 2.1), nonvertebral fracture (RR = 0.91; 95% CI, 0.77 to 1.2) or mortality (RR = 1.03; 95% CI, 0.2 to 5.2). However, the authors noted that fractures were reported as secondary outcomes and that the trials were not adequately powered to determine fracture risk.

A 1998 RCT (N = 4,432) examined the effect of oral bisphosphonate therapy on reduction of clinical fractures in postmenopausal women 54 to 81 years of age who had low BMD but no baseline vertebral or clinical fractures.[2] The study excluded women who had peptic ulcers; history of an endocrine disorder; significant renal, hepatic, or medical problems precluding three years of participation; prior bisphosphonate therapy; or estrogen or calcitonin use within the preceding six months. Patients were randomized to alendronate, 5 mg per day for two years, then 10 mg per day for the remainder of the trial, or

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Author disclosure: No relevant financial affiliations.

placebo. Treatment was continued for four years, then participants were stratified by baseline T-scores for subgroup analysis. There was no significant difference in fractures when comparing the whole treatment group to the control group. However, the subgroup of women whose baseline femoral or vertebral T-score was less than –2.5 had a significant reduction in clinical fractures (relative hazard [RH] = 0.64; 95% CI, 0.5 to 0.82; number needed to treat = 15). There was a significant decrease in radiographically diagnosed vertebral fractures in the whole treatment group, regardless of baseline BMD (RH = 0.56; 95% CI, 0.39 to 0.8).

A post-hoc analysis of a 2006 RCT (N = 1,099) included in the meta-analysis discussed previously evaluated the effect of BMD on the incidence of fractures with continuation or cessation of alendronate (10 mg per day) in women who initially received five years of treatment.[3] Compared with discontinuing therapy, continuation reduced nonvertebral fractures only in the group with femoral neck T-scores of –2.5 or less (RR = 0.50; 95% CI, 0.26 to 0.96), but not in the group with T-scores greater than –2.5. This conclusion is limited by the small numbers of fractures in the trial and by the nature of post-hoc analyses, in which final data are reexamined in ways that were not intended in the initial study design.

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