Zoledronate every 18 months for 6 years in osteopenic postmenopausal women: effects on fractures and non-skeletal endpoints

Authors: I. Reid[1, 2], A. Horne[1], B. Mihov[1], A. Stewart[1], E. Garratt[1], M. Bolland[1], S. Bastin[2], G. Gamble[1]

Affiliations: 1. University of Auckland 2. Auckland District Health Board

Bisphosphonates prevent fractures in patients with osteoporosis, but their efficacy in women with osteopenia is unknown. Most fractures in postmenopausal women occur in osteopenic individuals, so if pharmaceutical intervention is to impact significantly on total fracture numbers, therapies with efficacy in osteopenic postmenopausal women are needed.

We report a double-blind trial of 2000 osteopenic, postmenopausal women, randomly assigned to receive 4 infusions of either zoledronic acid (zol) 5mg, or normal saline at 18-month intervals. Each was followed for 6 years. Monthly vitamin D supplements were provided but not calcium supplementation. Women aged >65 years with hip T-scores between -1.0 and -2.5 were recruited.

Baseline age was 71 (SD 5) years and femoral neck T-score -1.5 (0.5). The primary endpoint of osteoporotic fracture (i.e. osteoporotic non-vertebral fractures plus morphometric vertebral fractures) occurred in 190 women in the placebo group (227 fractures) and in 122 women in the zol group (131 fractures), hazard ratio (HR) 0.63 (95%CI 0.50, 0.79; P < 0.0001). The number needed to treat to prevent one woman fracturing was 15. Non-vertebral osteoporotic fractures (HR 0.66, P = 0.0014), symptomatic fractures (HR 0.73, P<0.0027), vertebral fractures (odds ratio 0.45, P = 0.0018), and height loss (P<0.0001) were also reduced in the zol group.

There were 41 deaths in the placebo group and 27 in the zoledronate group (odds ratio 0.65, 95%CI 0.40, 1.05). Rate ratios for adverse events were: myocardial infarction 0.6 (0.3, 0.9), composite vascular endpoint 0.7 (0.5, 0.99), cancer 0.7 (0.5, 0.9), and breast cancer 0.6 (0.3, 0.98).

Conclusions: Zol prevents fractures in osteopenic older women, substantially broadening the target population for pharmaceutical intervention to prevent fractures. The beneficial effects seen on cancer and vascular disease are consistent with data from previous studies and suggest that zol should be formally trialled for the prevention of these conditions.