

# Combination and sequential therapy with PTH and bisphosphonates

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**Keywords:** PTH, Bisphosphonates, BMD, Fracture

Therapies that combine anabolic agents, such as PTH, with anti-resorptive agents, such as bisphosphonates, offer the potential for synergistic benefits for patients at high risk of fracture. Although fracture endpoint studies exist for monotherapy with either bisphosphonates or PTH, such studies do not exist for treatment strategies involving combined or sequential use of PTH and bisphosphonates, and only studies with surrogate endpoints currently exist.

Compared to bisphosphonate therapy alone, bisphosphonate therapy following PTH therapy results in greater gains in spine BMD. For example, in a small clinical trial, Rittmaster found that the mean increase in spine BMD after one year of daily PTH (1-84) followed by one year of alendronate (14%), was significantly greater than after one year of placebo injections followed by one year of alendronate (6%).

The hypothesis that concurrent treatment with PTH and bisphosphonate might increase areal and volumetric BMD to a greater extent than either agent alone has been tested in several trials, including the PaTH study. Compared to postmenopausal women who received PTH (1-84) or alendronate alone, women randomized to the combination of daily PTH plus daily alendronate had similar one-year gains in spine

BMD (5-6%). Conversely, PTH alone resulted in significantly greater increases in volumetric BMD of the spine as assessed by QCT. Similarly, there was no evidence that the combination of PTH + alendronate had a greater beneficial effect on hip BMD than either PTH or alendronate alone.

With regards to PTH following chronic anti-resorptive therapy, non-experimental evidence suggests that PTH therapy following chronic raloxifene use results in greater increases in BMD compared to PTH therapy following chronic alendronate therapy. In a study of postmenopausal women from a large HMO, spine BMD increased to a greater extent among postmenopausal women given PTH for 18 months in place of chronic raloxifene therapy (10.2%), compared to women given PTH in place of chronic alendronate therapy (4.2%), but there were no persistent differences in hip BMD or biochemical markers of bone turnover.

In summary, clinical studies have found that PTH followed by alendronate supports a continued increase in BMD and that the combination of PTH and alendronate does not increase bone mass more than either agent alone. Lastly, PTH after chronic alendronate therapy effectively increases BMD, but perhaps less so than after chronic raloxifene use.

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The author receives research funding from Merck, SKB, and NPS.

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Accepted 4 August 2004