

Treatment of osteoporosis with Teriparatide rhPTH(1-34)

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Currently, treatment with parathyroid hormone (PTH) is the only proven and approved method of increasing bone mass and improving bone architecture. This section reviews some selected aspects of treatment with Teriparatide rhPTH(1-34).

Teriparatide stimulates bone formation and remodeling thereby increasing BMD as measured by DXA and improves micro architecture (such as BV/TV, trabecular thickness and connectivity). The Fracture Prevention Trial in postmenopausal women with osteoporosis and prevalent fracture showed that 19 months of Teriparatide significantly reduced the risk of vertebral fractures by about 65% and non-vertebral fractures due to low trauma by 53%.

Optimal duration of therapy. The optimal duration of therapy is not known. The FDA limited use of Teriparatide to 2 years, because its safety had not been tested longer. However, data about markers of bone formation and resorption indicate that Teriparatide has its greatest effects on bone remodeling during the first 6 to 12 months of treatment. BMD continues to increase for a period of at least 30 months, and the non-vertebral fracture risk reduction also seems to continue to increase the longer the therapy was.

Toxicology studies in rats showed longer dose and duration of therapy correlated with the appearance of osteosar-

comas. However, that data can not be translated directly into the clinical safety because humans have a weaker response to PTH than do rats. The rats received PTH during skeletal growth whereas it is used in late life in humans. In humans, 2 years of PTH constitutes about 2 or 3 % of life span compared with 30 to 80% for rats. Studies are underway to assess the safety of longer term therapy with PTH.

Monitoring therapy with Teriparatide. As noted above, Teriparatide increases BMD, but the increase in bone mass occurs in the presence an increase in bone turnover with opening of remodeling spaces and decreases the degree of mineralization of the new bone formed. Thus, it may be unreliable to use improvements in BMD as a gauge of the effectiveness of treatment. Perhaps bone formation markers such as P1NP or BAP may help to follow up patients since they increase very rapidly, as early as 1 month after therapy started, and there is a good correlation between those changes in bone forming markers and improvement in the end points of BV/TB and trabecular thickness.

In conclusion, Teriparatide increases bone formation and bone mass and reduces fracture risk by improving structural parameters of bone. This would be an ideal component of curative treatment for osteoporosis.

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