

LETTERS

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Probable osteosarcoma risk after prolonged teriparatide treatment: comment on the article by Saag et al

To the Editor:

Teriparatide is known to be effective in increasing levels of bone turnover biomarkers in institutionalized, mostly nonambulatory adults with severe developmental disabilities. Its use has been approved by the US Food and Drug Administration (FDA) only for adults (1). Contraindications to the use of teriparatide include the following: any hypercalcemic disorder, osteosarcoma, metastatic bone disease, Paget's disease of bone, pregnancy, and radiation therapy to the skeleton or to soft tissue in which a skeletal port is exposed. A toxicity that appears to be unique to animals and not applicable to human subjects is osteosarcoma; osteosarcoma has developed in rats that have been given very high doses of either teriparatide or parathyroid hormone 1–84 for prolonged periods of time (2–4). It is unlikely that this animal toxicity is related to human skeletal physiology (5,6), but the FDA issued a black box warning with the approval of teriparatide. Treatment with teriparatide is approved by the FDA for a limited duration of 18–24 months, and in many European countries approval is limited to 18 months.

In some recent studies, the period of treatment with teriparatide was prolonged to 24–30 months (1,7). It has been reported that a longer treatment period may have a role in the development of various pathologies in animals, one of which is osteosarcoma (3). Although this has not been observed in humans to date, longer-term use of teriparatide, especially in the young population that makes up a great proportion of patients with glucocorticoid-induced osteoporosis, may cause risks. Because the exact relationship between the occurrence of osteosarcoma and the duration of treatment has not been clearly elucidated, it is difficult to determine an exact duration of treatment after which risk might develop. The most significant problem that patients will experience is not drug tolerance, but malignancy.

In the study by Saag et al published in the November 2009 issue of *Arthritis & Rheumatism* (8), teriparatide was used for up to 36 months in a patient population with a short duration of osteoporosis, which carries more prominent risks. We believe this prolonged treatment may have increased the risk of osteosarcoma occurrence. Although it has been reported that the teriparatide-related risk of osteosarcoma development is low (9), there are still no clear scientific data, and the general recommendation about this treatment is to closely follow up patients who have risk factors (10). Therefore, we have the following questions about the study by Saag et al: How was the treatment duration planned? Were the patients evaluated for risk of osteosarcoma development before the study? Did the authors experience difficulties with the ethical approval process? And how will the study patients be followed up prospectively in terms of osteosarcoma risk?

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Reply

To the Editor:

We thank Drs. Tastekin and Zateri for their interest in our study. They have asked a few questions regarding the design and clinical context of this 36-month study of teriparatide and alendronate in ambulatory subjects with glucocorticoid-induced osteoporosis. The study was preplanned with a double-blind treatment duration of 36 months (18-month primary phase [Saag KG, Shane E, Boonen S, Marin F, Donley DW, Taylor KA, et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. *N Engl J Med* 2007;357:2028–39] followed by an 18-month continuation phase [with the 36-month results reported in the article in *Arthritis & Rheumatism*]). The 18-month continuation phase was intended to gather addi-