Role of Zoledronate in Aromatase Activity Should Be Considered in Future Studies

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Disclosures of potential conflicts of interest may be found at the end of this article.

I read with curiosity the recently published article in *The Oncologist* by Valachis et al. [1]. The authors skillfully reviewed the literature on fracture and survival rates with the use of zoledronate versus no or delayed use in the adjuvant treatment of women with early stage breast cancer. This review is helpful for showing the positive role of zoledronate in the treatment of patients with breast cancer. It should be noted, however, that zoledronate may have additional effects on the suppression of aromatase activity and plasma estrogen levels, according to results gleaned from other studies.

Adjuvant breast cancer clinical trials have evaluated the intravenous bisphosphonate zoledronate. Strong evidence from the Zometa-Femara Adjuvant Synergy Trials (Z-FAST and ZO-FAST) shows that aromatase inhibitor-associated bone loss is manageable and preventable with bisphosphonates, especially zoledronate [2, 3]. In another adjuvant early breast cancer study, the Analysis of the Austrian Breast and Colorec-

tal Cancer Study Group Trial-12, zoledronate was significantly associated with improvements of cancer outcomes in premenopausal women [4]. It was previously shown that zoledronate prevented deep bone loss when goserelin was combined with tamoxifen or anastrozole [5]. In a similar study, Schech et al. [6] showed that the combination of letrozole and zoledronate caused increased inhibition of aromatase activity compared with letrozole alone. Zoledronate can inhibit the aromatase enzyme by inhibition of serine phosphorylation.

Considering the additive effect of zoledronate on aromatase activity, plasma estrogen levels should be investigated or controlled for in future trials that seek to elucidate the mechanisms and components responsible for the recently reported effects of zoledronate in women with breast cancer.

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