Adjuvant Therapy With Zoledronic Acid and Menopausal Status

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

We read with interest the recent article by Valachis et al. in *The Oncologist* [1]. The authors analyzed the results of the published literature for adjuvant therapy with zoledronic acid (ZA) in patients with breast cancer. They concluded that ZA as adjuvant therapy in breast cancer patients appears to have a benefit for overall survival (OS) over placebo or no treatment, but they did not show a benefit for disease-free survival (DFS). These results conflicted with a recent meta-analysis conducted by Yan et al. [2], who focused on the same research question.

The authors of the present study did not perform a subgroup analysis based on menopausal states because heterogeneity in the definition of postmenopausal status makes comparisons unreliable [1]. It should be mentioned that the benefits of ZA for OS and DFS were observed only in postmenopausal patients and especially in those who were past menopause for more than 5 years. In the Adjuvant Zoledronic Acid to Reduce Recurrence or "AZURE" trial [3], among patients who had undergone menopause more than 5 years earlier, the DFS rates were 78.2% in the ZA group and 71.0% in the control group, and the OS rates were 84.6% in the ZA group and 78.7% in the control group. In the Zometa-Femara Adjuvant Synergy Trial ZO-FAST [4], referring to postmenopausal

patients, the DFS rates were 94.5% in the upfront ZA group and 90.8% in the delayed ZA group, and the OS rates were 97.0% in the upfront zoledronic group and 95.1% in the delayed ZA group. The Analysis of the Austrian Breast and Colorectal Cancer Study Group Trial-12, or the "ABCSG-12" trial [5], involved premenopausal patients who had received ovarian function suppression and thus should be considered postmenopausal patients. That study showed DFS rates of 89.1% in the ZA group and 85.4% in the control group and OS rates of 96.3% in the ZA group and 94.6% in the control group. No benefit for OS and DFS with ZA use was seen in premenopausal patients in any of the included studies.

In our opinion, the present study by Valachis et al. [1] sends an important message that ZA as adjuvant therapy in breast cancer patients had a beneficial effect on OS. Our previous study of adjuvant therapy with clodronate acid in patients with breast cancer indicated that adjuvant treatment with clodronate may improve OS in patients with early breast cancer [6]. Further study with analysis of subgroups by age or menopausal status should be performed to investigate adjuvant therapy with bisphosphonates in breast cancer patients.

DISCLOSURES

The authors indicated no financial relationships.

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