Aromatase Inhibitors and Postmenopausal Breast Cancer Patients with Tamoxifen-Induced Endometrial Pathology

To the Editor: We have read with great interest the recently published article by Gerber et al. (1) on the potential endometrial benefit of anastrozole given to postmenopausal breast cancer patients with tamoxifen-induced endometrial pathology. Their study showed that the switch to anastrozole significantly reduced the need for a second invasive gynecologic procedure for recurrent vaginal bleeding or endometrial thickening.

We believe that their conclusion is also true for the other two aromatase inhibitors: letrozole and exemestane. In a prospective study of postmenopausal breast cancer patients published a year ago (2), we showed using transvaginal ultrasonography the nonstimulatory endometrial effect of both steroidal and nonsteroidal aromatase inhibitors. Moreover, our study also showed that 3 months of an aromatase inhibitor significantly decreased endometrial thickness and uterine volume in patients previously exposed to tamoxifen. In addition to what the authors mentioned in their article about the preliminary findings on the potential of letrozole to decrease tamoxifen-induced endometrial thickening in 17 evaluable patients (3), data are also available for the endometrial effect of exemestane. The Intergroup Exemestane Study recently presented endometrial data from 219 patients showing that switching to exemestane resulted in a significant reduction in the proportion of patients with an endometrial thickness ≥5 mm. This switch also resulted in the reversal of subclinical uterine abnormalities associated with tamoxifen (4).

Another point we would like to refer to is the difference in management between users of tamoxifen and an aromatase inhibitor in case there is abnormal vaginal bleeding. Whereas long-term tamoxifen users always need a gynecologic workup to exclude malignancy, including transvaginal ultrasonography, and an invasive gynecologic procedure, such as hysteroscopy and dilation and curettage, this is not necessary for users of aromatase inhibitors. Given the nonstimulatory effect of aromatase inhibitors on the endometrium, it is logical that a conservative strategy should be used if the transvaginal ultrasonography–measured endometrium is <5 mm. As shown by Gerber et al. (1), endometrial atrophy was present in all four patients in the anastrozole group who required repeat dilation and curettage due to vaginal bleeding. However, although we recognize endometrial atrophy as the most important reason for vaginal bleeding on aromatase inhibitors, it is prudent to note that endometrial abnormalities may exist even in the presence of a thin endometrium. Taking this into account, we believe that a Pipelle endometrial biopsy should be the standard of practice when a woman presents with vaginal bleeding while using an aromatase inhibitor even with a thin and regular endometrium on transvaginal ultrasonography. In such case, the risk for endometrial cancer is low. Therefore, any other invasive gynecologic procedure as a first step in the work up is not justified (5).

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