Leuprolide Acetate Plus Aromatase Inhibition for Male Breast Cancer

To the Editor: Approximately 1% of breast cancer occurs in male patients, yet little information is available on the optimal treatment of this disease. Male patients with breast cancer are more likely than female patients to have tumors positive for estrogen and/or progesterone receptors. However, the hormonal environment in male patients differs from that in female patients; thus hormone therapies that are effective in women may or may not be effective in male patients. In particular, the role of aromatase inhibitors in male patients is unclear. Preclinical data suggest that aromatase inhibitors may be less effective in men. In animal models, chronic administration of aromatase inhibitors was associated with significant increases in follicular stimulating hormone and testosterone and no change in levels of estradiol. A possible explanation for this finding is that the increase in follicular stimulating hormone and testosterone could lead to an increase in substrate for aromatization via a feedback loop. Aromatase inhibitors have also been tested in healthy male volunteers and resulted in a 50% decrease in estradiol but an increase in testosterone levels. To our knowledge, seven cases of men with breast cancer treated with aromatase inhibitors have been reported in the literature. One series of five patients reported no responses, and two case reports have documented responses to aromatase inhibitors.

We now wish to report two cases of male patients treated with a combination of leuprolide acetate and aromatase inhibitors. The rationale for this combination was that the addition of leuprolide to an aromatase inhibitor could inhibit the feedback loop to the hypothalamus and pituitary glands and thus achieve better suppression of estrogen.

The first patient was a 56-year-old man with breast cancer metastatic to the lungs. He was initially diagnosed with a left-sided T1cN0M0 invasive ductal carcinoma, estrogen- and progesterone-receptor–positive, HER-2–negative by fluorescence in situ hybridization. He was treated with a left modified radical mastectomy, adjuvant radiotherapy, and adjuvant tamoxifen. After 2 years, he was found to have a recurrence in an ipsilateral infracavicular lymph node, which was treated with radiation therapy. His hormone therapy was changed to anastrozole. Ten months later, he developed lung metastases. Anastrozole was treated with radiation therapy. His hormone therapy was changed to exemestane. On re-evaluation 13 weeks later, representative lesions in the right lower lobe measured 13.5 mm, and in the right upper lobe measured 13.5 mm. At this point, the leuprolide was continued and letrozole was added. Eight weeks later, the index lesion in the right upper lobe had increased from 16.7 mm to 20.2 mm (37% decrease) and the right lower lobe measured 13.5 mm × 10.2 mm (40% decrease). The patient has currently completed 22 weeks of treatment on leuprolide and letrozole and continues without progression.

The second patient was a 49-year-old man with breast cancer metastatic to the lungs and bone. He was initially diagnosed with a T1c invasive ductal carcinoma. He was treated with modified radical mastectomy and had 4 of 17 involved axillary lymph nodes. The tumor was estrogen- and progesterone-receptor positive, HER-2–negative. He was treated with four cycles of adjuvant paclitaxel and four cycles of fluorouracil, doxorubicin, and cyclophosphamide (FAC), adjuvant radiation, and adjuvant tamoxifen. Four years later, he developed metastases to bone, lung, and lymph nodes. A metastatic lesion was biopsied and was estrogen- and progesterone-receptor–positive. Zoledronic acid was started. He was treated with capecitabine for 10 months with initial response followed by progression. He received palliative radiation to the thoracic spine and left eighth rib. At that point, he had bilateral pulmonary nodules, the largest measuring 10.2 mm. His systemic therapy was changed to leuprolide acetate and anastrozole. At re-evaluation 9 weeks later, he had near complete resolution of pulmonary nodules (with only mild residual ground glass opacities) and evidence of bone healing. He has currently completed 6 months of treatment on leuprolide and anastrozole and remains without progression.

We have reported two cases of responses to leuprolide acetate and aromatase inhibitors in men with metastatic breast cancer. Of note, the first case had failed to respond to either agent as a single agent. We believe that this combination deserves further investigation. Currently, the Southwest Oncology Group has activated S0511, which evaluates the combination of anastrozole and goserelin in men with hormone-receptor–positive metastatic breast cancer. In addition to assessing response rates and survival, this protocol will measure hormone levels and will bank tissue and serum samples. Accrual to this new protocol will be crucial to making improvements in the care of men with breast cancer.

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REFERENCES

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