Endocrine Therapy for Breast Cancer

By Aman U. Buzdar, MD [4]

Endocrine therapy is the oldest form of treatment for metastatic breast cancer. The availability of numerous new endocrine agents during the past 10 years has led to significant changes in the use of this form of therapy. This article identifies appropriate candidates for endocrine therapy and describes various treatment options for different subsets of patients with metastatic disease. Overall, Dr. Pritchard does an excellent job of summarizing this information in her article. However, a few shortcomings of the article need to be addressed.

Points Requiring Further Comment

1. The article does not provide a comparison of the two antiestrogens approved for the treatment of metastatic disease in North America, ie, tamoxifen (Nolvadex) and toremifene (Fareston). The author fails to state that both agents have similar antitumor activity. There is cross-resistance between the two agents, and, thus far, no evidence suggests the superiority of toremifene over tamoxifen. Also omitted is the fact that there are no appropriate long-term data on the efficacy of toremifene in the adjuvant setting.

2. Exemestane (Aromasin) is a second-generation steroidal aromatase inhibitor that acts by suicidal inhibition of the aromatase enzyme. This drug has been evaluated as second-line therapy in postmenopausal women in a phase III study.[1] All of the patients had received prior treatment with tamoxifen and, upon disease progression, were included in the study. The data from this phase III study demonstrate a similar degree of antitumor activity with exemestane as has been observed with the other two aromatase inhibitors, anastrozole (Arimidex) and letrozole (Femara). Of significant interest are data from limited phase II studies showing that exemestane has antitumor activity in patients previously treated with aminoglutethimide. No data currently exist regarding the efficacy of anastrozole or letrozole following treatment with exemestane. Dr. Pritchard fails to point out that the appropriate sequence of treatment may be an Imidozole followed by exemestane.[2] This approach would enhance the treatment armamentarium for metastatic disease, as exemestane has significant antitumor activity and a better safety profile than the pro-gestins, which are currently used as third-line therapy in this subset of patients.

3. The article contains a lengthy discussion of combined hormonal therapy. However, the data are too heterogeneous, and the studies cited do not have appropriate statistical strength to recommend combined hormonal therapy in the metastatic setting at present. Sequential use of these agents is recommended until more convincing data become available to change this practice.

4. In the adjuvant setting, ongoing trials are evaluating the role of combined hormonal therapy. However, results of those studies are not yet available.

5. In postmenopausal patients who are estrogen receptor positive, the combination of chemotherapy plus tamoxifen is superior to tamoxifen alone. This point is not clearly made in the article, however.

6. The article includes a brief discussion of data comparing anastrozole vs tamoxifen as front-line therapy.[3] (These data became available after Dr. Prichard’s “Meet the Professor”
session at the 1999 American Society of Clinical Oncology (ASCO) meeting, and were obviously added by the author to update her talk.) These data suggest the first new treatment option for postmenopausal women in 30 years. In patients with estrogen receptor positive tumors, anastrozole has antitumor activity that is superior to that of tamoxifen, and it also has a better safety profile than tamoxifen.

Thus, currently, anastrozole could be considered as initial therapy for metastatic breast cancer in postmenopausal patients who have an estrogen receptor-positive tumor. However, detailed reports of the data are needed before further comments can be made regarding these two studies.

**Summary**
The availability of a number of new agents and a better understanding of endocrine treatment have expanded the treatment options for women with metastatic breast cancer. Endocrine therapies can palliate the symptoms of patients who have an estrogen-dependent tumor. Sequential use of endocrine agents can control the disease for an extended period in this subset of patients.

**References:**


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