Role of anti-aromatase agents in postmenopausal advanced breast cancer

Abstract Purpose: Endocrine therapy is a well-recognized approach to the treatment of postmenopausal patients with advanced breast cancer, particularly those with estrogen receptor-positive tumors. The availability of anti-aromatase agents, both reversible (nonsteroidal) and irreversible (steroidal), provides clinicians with additional hormonal treatment options. Methods: A MEDLINE search was conducted to identify studies that evaluated anti-aromatase therapy in the treatment of postmenopausal women with advanced breast cancer. In selecting studies, priority was given to randomized, controlled trials. Results: Tamoxifen is the standard first-line therapy for advanced breast cancer. However, recent results have demonstrated the efficacy of newer anti-aromatase agents in this setting. Among patients who have progressed after tamoxifen therapy, anti-aromatase agents have emerged as first choice therapy based on their better tolerability and improved efficacy compared with megestrol acetate. Exemestane and anastrozole (irreversible and reversible anti-aromatase agents, respectively) have demonstrated survival benefits over megestrol acetate in second-line therapy. Anti-aromatase agents have also demonstrated efficacy in patients who have failed multiple hormonal therapies. Based on these data, an algorithm for the treatment of postmenopausal women with advanced breast cancer is proposed. Conclusions: The enhanced tolerability and superior efficacy of anti-aromatase inhibitors compared with megestrol acetate has resulted in these agents becoming the endocrine treatment of choice for women with advanced breast cancer who have progressed after tamoxifen treatment. The increased use of tamoxifen in the adjuvant setting and the demonstrated activity of aromatase inhibitors in first-line therapy will further increase the role of these agents.

Keywords Postmenopausal breast cancer · Hormone therapy · Anti-aromatase agents

Introduction

Although there have been new developments in the treatment of metastatic breast cancer over the past few years, the disease still presents an important challenge for physicians. Current treatment strategies provide substantial palliation of symptoms, but have limited impact on survival and are often associated with objectionable side effects. Due to the large variety of clinical manifestations, a number of therapeutic modalities are used in treating advanced disease. Chemotherapy, hormonal therapy, surgery, and radiation therapy are all components of a metastatic breast cancer treatment strategy and, in general, are all utilized at some point during the course of the disease. Hormone therapy has long been accepted to be amongst the most successful treatments for breast cancer and a majority of postmenopausal patients presenting with metastatic disease will benefit from some form of endocrine therapy.

The availability of the anti-aromatase therapies, a novel class of estrogen-deprivation agents, offers clinicians a more selective approach to the hormonal treatment of breast cancer. The enhanced efficacy and tolerability of this approach have been demonstrated – several of these agents exhibit a survival advantage over current standard second-line therapy [5, 17]. The availability of anti-aromatase agents with different mechanisms of action now extends even further the range of effective agents from which a physician can select. Although the most effective sequence or combination in which to use these agents has yet to be elucidated, it is clear that these agents will play a major role in the future treatment of postmenopausal patients with metastatic breast cancer.


**Establishing the course of treatment**

For a postmenopausal woman presenting with metastatic disease, the initial decision regarding the course of treatment is based on a number of well-defined prognostic factors (Fig. 1) [11, 13]. Local therapy (e.g. surgery, radiation therapy) is beneficial in patients with a single focus of symptomatic disease or in the event of local crisis (impending fracture, spinal cord compression). Systemic therapy is first-line treatment for patients with multiple sites of recurrence and/or visceral disease not easily treated by local therapy. The choice between hormone therapy and chemotherapy is based on a set of patient factors including hormone receptor status, disease-free interval, age, and quality of life determinants [12].

Chemotherapy is the treatment of choice for hormone receptor-negative tumors, rapidly progressing visceral lesions, or tumors that have become refractory to hormonal treatment [10, 12, 13]. However, the significant toxicity of this approach is a major drawback, even with the advent of hematopoietic growth factors and better antiemetics. In addition, repeated use of chemotherapy following an initial treatment failure has limited effect on survival. Hormone therapy is the first choice of treatment for women who have limited and non-life-threatening disease, especially those with no

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**Fig. 1** Treatment algorithm for advanced postmenopausal breast cancer.