

Introduction: The Status of Metastatic Breast Cancer Management

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Women fear breast cancer for many reasons. They fear the disease, the associated disfiguring surgery, and the short- and long-term effects of therapy. A primary fear is death from metastatic breast cancer (MBC). Breast cancer remains the most common malignancy among women in the United States and is second only to lung cancer as a cause of cancer death. The American Cancer Society (2008) estimated that 182,460 new cases of breast cancer were diagnosed and 40,930 women died of invasive MBC in the United States in 2008. The five-year overall survival rate for women with MBC is 27% (American Cancer Society). Cytotoxic chemotherapy and newer targeted agents are appropriate for patients with hormone-refractory disease, rapidly progressive visceral disease, or early relapse after adjuvant therapy, according to guidelines issued by the National Comprehensive Cancer Network (2008).

Although the death rate from breast cancer has been decreasing steadily since 1990—primarily because of early detection and the development of new therapies—a great need still remains for additional therapeutic alternatives for certain patient subpopulations, especially women with MBC. Drug resistance typically has a crucial impact on the treatment of MBC and has limited the long-term survival in that population.

Selection of appropriate treatment for MBC begins with an accurate pathologic assessment. A major focus of oncology nursing is to teach patients what each component of their pathology reports signifies and how the information provides valuable guidance in selecting appropriate and effective treatment (Hayes, 2008).

For the majority of women with MBC, treatment is aimed at palliation and prolongation of survival, rather than cure, with the best possible quality of life. Given the wide range of choices of available chemotherapeutic, biologic, and hormonal agents, therapy must be individualized. Several factors may affect treatment choice, including a patient's performance status, physician preference, adherence to therapy, drug administration route, comorbidities, drug toxicities, tumor characteristics, hormonal status, efficacy, and prior exposure to the same drug class. In some cases, single, sequential agents may be the most appropriate choice; in others, a combination of agents might be the most effective and appropriate choice.

A paradigm shift has occurred in the management of MBC since the development of targeted therapies. An improved understanding of breast tumor cell biology and molecular genetics

(see Figure 1) is enabling researchers to design cancer therapies that are tailored to the unique characteristics of each patient and her tumor. Targeted therapy may have greater efficacy and fewer side effects than conventional chemotherapy and may ultimately lead to improved survival and quality of life in that population.

In MBC, trastuzumab was the first monoclonal antibody to become available for women with HER2-positive breast cancer. That research development signaled the clinical potential of monoclonal antibodies, and targeted therapies became a reality. After researchers established trastuzumab's efficacy as a single agent in refractory MBC, investigators were challenged to determine how to combine it with conventional cytotoxic chemotherapy and, subsequently, with other monoclonal antibodies or other small-molecule-targeted therapies. The findings have provided valuable insight for the development of other targeted therapies.

When considering targeted therapies, accurately identifying the molecular target is essential to taking advantage of their selectivity and to determining the appropriate patient population who will benefit from the approach. Although the drugs offer some therapeutic benefits over conventional cytotoxic agents alone, they require some trade-offs. Side effects include cardiotoxicity as well as gastrointestinal and dermatologic changes, which sometimes limit which patients should receive or can tolerate such agents. Other considerations in selecting treatment, such as the propensity of MBC to recur in the central nervous system, should be anticipated and countered with appropriate therapy combinations. Eventually, what is learned in the advanced-disease setting regarding dose, scheduling, and combinations will be able to be applied to treatment of early breast cancer.

Clinical trials of targeted therapies, such as tyrosine kinase inhibitors, have demonstrated benefits in patients with advanced disease and may delay resistance. The tyrosine kinase inhibitor

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