The Status of Chemotherapy in Metastatic Breast Cancer: Insights for the Advanced Practitioner

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Authors' disclosures of conflicts of interest are found at the end of this article.

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Breast cancer is the most frequently diagnosed cancer in the United States and ranks second as the most common cause of cancer-related death among women (Siegel et al., 2020). According to American Cancer Society (ACS) estimates, approximately 276,480 new cases of breast cancer would have been diagnosed in 2020, and greater than 42,000 deaths would be attributed to breast cancer (ACS, 2020). Although only 7% of all cancer-related deaths are from breast cancer every year, it is the leading cause of death among women between the ages of 40 and 49 years (Siegel et al., 2020). The death rate associated with breast cancer, however, has decreased by 1.3% annually from 2013 to 2017.

While improvements in treatment and management coupled with early detection have accounted for the decreased death rate, as of January 2020, there were more than 3.5 million women with a history of breast cancer in the United States (ACS, 2020). Indeed, a vast majority of women with newly diagnosed breast cancer have localized or regional disease that is associated with almost 99% to 85.7% 5-year survival rates, respectively (ACS, 2020).

The primary treatment goal for patients with early-stage disease is to reduce the probability of recurrence and spread with primary surgery (lumpectomy or mastectomy) of the breast and regional nodes, with or without radiation therapy and/or in conjunction with neoadjuvant and adjuvant systemic therapy. Despite the successes of these approaches, up to 30% of women with early-stage, nonmetastatic breast cancer will eventually develop distant metastatic disease, and almost 6% of newly diagnosed women have metastatic breast cancer (MBC) at diagnosis (ACS, 2020; Early Breast Cancer Trialists' Collaborative Group, 2005). It has been estimated that more than 150,000 women are living with MBC, among whom 3 in 4 patients were initially diagnosed with earlier stage disease (Mariotto et al., 2017). Unfortunately for these women, MBC is not curable, and while meaningful improvements have been reported due to the introduc-

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tion of newer therapies, the 5-year survival rates for MBC are at 27% (ACS, 2020).

TREATMENT

The goals of therapy for MBC are to improve progression-free survival and improve quality of life by reducing cancer-related symptoms and treatment-related toxicities (Harbeck & Gnant, 2017). Over the years, an improved understanding of the molecular biology of breast cancer has led to the identification of three major subtypes based on the presence or absence of molecular markers for estrogen or progesterone hormone receptors and the expression level of human epidermal growth factor receptor 2 (HER2). These subtypes are hormone receptor positive/HER2 negative (70% of patients), HER2 positive (15%–20% of patients), and triple negative (tumors lacking all three standard molecular markers; 15% of patients). The therapeutic approach is chosen based on tumor subtype, with hormone receptor–positive/HER2-negative cancers initially treated with endocrine therapy–based regimens, HER2-positive disease being treated with HER2-targeted therapy in combination with chemotherapy and/or endocrine therapy, and single-agent chemotherapy being used for triple-negative tumors (Waks & Winer, 2019).

Importantly, multiple lines of therapy and a combination of agents are generally needed over the treatment course due to disease relapse and treatment resistance, and this ultimately involves the use of chemotherapeutic agents (Waks & Winer, 2019). For example, cytotoxic chemotherapy can be used up front among symptomatic patients, those with triple-negative disease, and those with progressive bone and/or visceral disease, but can also be provided as a later line of therapy for patients who have become refractory to endocrine therapy or earlier lines of therapy, and as a palliative measure during end-of-life care (Waks & Winer, 2019).

Overall, in spite of the advent of biologic and targeted agents, chemotherapy continues to be the mainstay of treatment regimens for MBC (Feinberg, 2019; Schneeweiss et al., 2015). Given that over 60 different therapies are currently available for MBC and that ongoing clinical trials are investigating the role of novel agents and varied combinations, therapeutic decisions in MBC have become all the more complex (National Comprehensive Cancer Network [NCCN], 2020). Moreover, multiple factors influence treatment decisions in MBC, which include the comparative safety and efficacy of agents, convenience of administration, impact on quality of life, patient preferences, and cost effectiveness. Thus, a one-size-fits-all approach cannot be applied for patients with MBC, and advanced practitioners need to rely on interprofessional collaboration, evidence-based guidelines, and real-world evidence to design personalized treatment plans for individual patients (NCCN, 2020).

To that end, a multidisciplinary care team is crucial to ensure adherence to therapy and address patient barriers and concerns while harnessing a shared decision-making approach. The following reviews, "Chemotherapy Treatment Considerations in Metastatic Breast Cancer" and "The Use of Real-World Evidence for Oral Chemotherapies in Breast Cancer" summarize the latest updates in the use of chemotherapy in MBC with patient-focused implications for advanced care practice.

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Disclosure

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