Metastatic Breast Cancer Epidemiology and Management With a Focus on Taxanes

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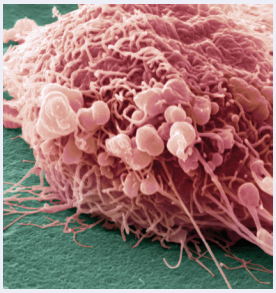

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Although considerable treatment advances have been made since the early 2000s, metastatic breast cancer (MBC) continues to provide challenges for patients and healthcare providers. The responsibilities of nurses regarding the management of MBC are extensive. Among other things, nurses must provide patient education, understand treatment administration, and have the ability to perform patient assessments, as well as identify and manage symptoms. The taxanes paclitaxel, docetaxel, and *nab*-paclitaxel are a class of microtubule-stabilizing agents that are highly active against MBC but have many differences among them (e.g., formulation, administration, efficacy, tolerability profiles). Understanding those differences will aid in improving the overall patient experience. This supplement provides a historical overview of taxanes, examines the differences in their administration, and defines their efficacy and safety profiles and effects on patient quality of life. In addition, methods for assessing taxane-induced neuropathy are discussed from the nursing perspective, and treatment considerations for older adult patients with MBC are provided.

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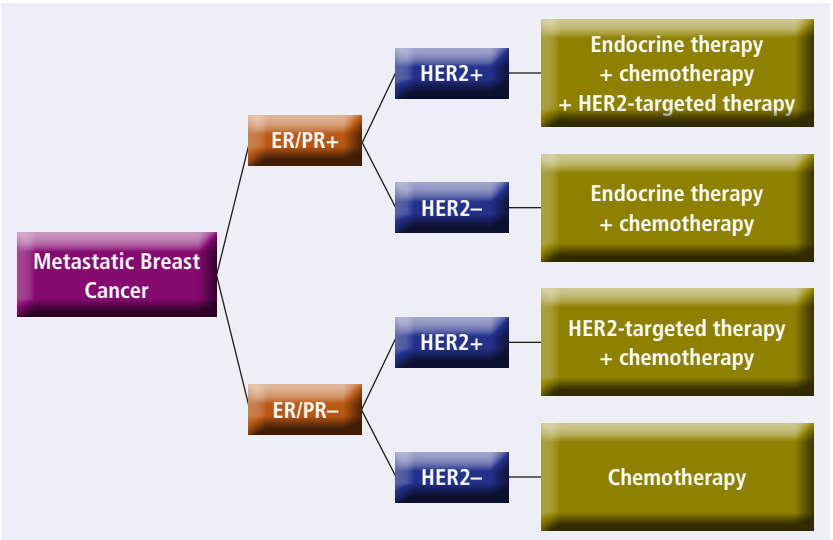
Digital Object Identifier:10.1188/13.CJON.S1.5-8

Breast cancer remains the most common cancer among women worldwide (American Cancer Society, 2011, 2012). Despite a decline in the incidence of breast cancer in the United States since the early 2000s, an estimated 226,870 new cases of breast cancer were diagnosed and 39,510 women died of breast cancer in 2012 (American Cancer Society, 2012). Since the 1990s, improved screening and methods for detection have enhanced diagnosis of early disease (Berry et al., 2005); however, about 5% of patients will be diagnosed with metastatic disease (Howlader et al., 2012). The prognosis for those patients is poor, with a five-year survival rate of 23% compared with 84%–99% for those with early-stage breast disease (American Cancer Society, 2012). In addition, disease recurrence at a distant metastatic site is common, occurring in as many as 30% of women initially diagnosed with an earlier-stage breast cancer (Early Breast Cancer Trialists' Collaborative Group [EBCTCG], 2005).

In the absence of curative treatments for patients with metastatic breast cancer (MBC), the goal of therapy remains palliative (i.e., to improve or lessen symptoms, improve quality of life, prolong survival, and delay disease progression) (O'Shaughnessy, 2005). Current management strategies must maintain a fine balance among controlling disease, prolonging survival, and maintaining quality of life. Breast cancer is a complex and heterogeneous disease composed of multiple distinct subtypes (Curtis et al., 2012). As a result, care is individualized based on tumor characteristics, including hormone receptor (HR) and HER2 status, previous therapies, patient performance status, extent of disease, presence of symptoms, and patient preference (Hurtig, 2010; O'Shaughnessy, 2005) (see Figure 1).

Hormone therapy with aromatase inhibitors (anastrozole, letrozole, or exemestane) or antiestrogen agents (tamoxifen or fulvestrant) has demonstrated efficacy in patients with tumors positive for estrogen or progesterone expression (Bergh et al., 2012; Bonneterre et al., 2000; Mouridsen et al., 2003; Paridaens et al., 2008). Patients who experience disease progression on hormonal therapy may benefit from additional treatment with a different class of hormonal agent (Chia et al., 2008; Perey et al., 2007).



ER/PR—estrogen receptor/progesterone receptor

FIGURE 1. Simplified Treatment Paradigm for Metastatic Breast Cancer

Note. Based on information from National Comprehensive Cancer Network, 2012.

In patients with MBC who have HER2-positive disease, agents targeting the HER2 receptor, including trastuzumab, lapatinib, and pertuzumab, have demonstrated significant clinical benefit when used in combination with systemic chemotherapy with respect to reduction of tumor burden and prolongation of overall survival (National Comprehensive Cancer Network [NCCN], 2012). As with HR-positive disease, patients who experience disease progression on anti-HER2 therapy have been shown to derive a modest benefit from additional therapy with an alternate anti-HER2 therapy. For example, patients progressing on trastuzumab may benefit from therapy with lapatinib (Von Minckwitz et al., 2011).

For patients with MBC with HR-negative disease, those with HR-positive disease with symptomatic visceral metastases, or those who are refractory to hormone therapy, current guidelines recommend systemic chemotherapy (NCCN, 2012). Systemic chemotherapy, the mainstay of management for patients with MBC, can reduce tumor burden and has been shown to prolong survival and improve quality of life (NCCN, 2012). To date, several classes of cytotoxic chemotherapy with different efficacy and tolerability profiles are recommended for the treatment of MBC (see Table 1). Of the recommended agents, taxanes (paclitaxel, docetaxel, and *nab*-paclitaxel) have well-established efficacy and safety profiles in the treatment of MBC. With the advent of taxane therapy, patients with MBC requiring chemotherapy have experienced improved outcomes compared with previous standard-of-care regimens (Bishop et al., 1999; Gradishar et al., 2005, 2009, 2011; Nabholtz et al., 1993).

Taxanes for the Treatment of Metastatic Breast Cancer

Taxanes act by stabilizing microtubules, leading to inhibition of cell proliferation (Bettelheim, Brown, Campbell, & Farrell, 2010). One of the major differences among the taxanes is formulation; docetaxel (sanofi-aventis, 2010) and paclitaxel (Bristol-Myers Squibb, 2011) are formulated with solvents, whereas *nab*-paclitaxel (Celgene Corporation, 2012) is formulated with albumin. That difference in solvents translates to differences in toxicity profiles and administration concerns (Bristol-Myers Squibb, 2011; Celgene Corporation, 2012; sanofi-aventis, 2010). Nurses play a key role in monitoring taxane-related side effects and educating patients on the signs and symptoms of toxicities. For nurses, being aware of potential taxane-related symptoms, being able to recognize them, and understanding their management in patients with MBC is critical. In addition, nurses must encourage patients to be forthcoming about any symptoms they experience. Among the key issues with taxanes and other microtubule inhibitors, sensory neuropathy is a potential toxicity that, if not monitored, can leave a patient with permanent neuronal damage (Hausheer, Schilsky, Bain, Berghorn, & Lieberman, 2006; Pachman, Barton, Watson, & Loprinzi, 2011; Ribeiro et al., 2012). In addition, comorbid conditions may place a patient at increased risk for developing peripheral neuropathy; therefore, being aware of and educating patients on these potential issues is important (Schneider et al., 2012). Symptoms such as fatigue can indicate a potential hematologic issue (e.g., taxane-induced neutropenia, anemia) (Wicklin Gillespie, 2005). Those symptoms often are indicative of many underlying issues and may not always be recognized by the healthcare provider as key taxane-related toxicity concerns. Fortunately, a number of tools exist that can be used in the assessment of patients receiving taxane therapy. Toxicities associated with taxane therapy also can affect patient quality of life; therefore, the appropriate assessment and management of patients receiving taxane therapy can help to improve quality of life for many patients.

Aim of the Supplement

The intent of this supplement is to provide an overview of taxane therapy for the treatment of MBC. The first article discusses the evolution of taxanes in the treatment of MBC, including concerns with regard to the solvent used to formulate each taxane. The second article discusses the efficacy and safety profiles of each taxane in the first-line setting, along with administration and key tolerability issues of each taxane. The third article offers insight into the assessment and management of taxane-related neuropathy, including current assessment tools. The fourth article provides a case study and a commentary on taxane-related quality-of-life considerations from a nursing perspective. This supplement concludes with special considerations in the management of older adult patients with MBC. The goal is a greatly improved patient experience through a greater understanding of the chemotherapeutic agents used in the treatment of MBC.

TABLE 1. Current Agents Recommended for the Treatment of Metastatic Breast Cancer

Microtubule Inhibitors	Vinca Alkaloids	Alkylating Agents	Anthracyclines	Targeted Therapies	Antimetabolites	Topoisomerase Inhibitors
Agents						
Paclitaxel	Vinblastine	Cisplatin	Doxorubicin	Trastuzumab	5-Fluorouracil	Etoposide
Docetaxel	Vinorelbine	Cyclophosphamide	Epirubicin	Lapatinib	Gemcitabine	Mitoxantrone
nab-Paclitaxel	–	Carboplatin	–	Pertuzumab	Capecitabine	–
Eribulin	–	–	–	–	–	–
Ixabepilone	–	–	–	–	–	–
Major Toxicity Concerns						
Neuropathy	Neuropathy	Nephrotoxicity	Cardiotoxicity	Cardiotoxicity	Gastrointestinal	Cardiotoxicity
Myelosuppression	Myelosuppression	Myelosuppression	Tissue necrosis if extravasation during infusion	Pulmonary toxicity	Coagulopathy	Development of secondary acute myelogenous leukemia
Hypersensitivity (solvent-based agents[a])	Pulmonary toxicity	Hypersensitivity	Myelosuppression	Hepatotoxicity	Myelosuppression	Myelosuppression
Cardiotoxicity (eribulin)	Gastrointestinal toxicity	Urinary system toxicity (cyclophosphamide)	Infusion reactions	Infusion reactions	Nephrotoxicity	Neuropathy
Infusion reactions	Cardiotoxicity	Cardiotoxicity	–	–	–	–
–	Infusion reactions	Infusion reactions	–	–	–	–

[a] Paclitaxel and docetaxel

Note. Based on information from National Comprehensive Cancer Network, 2012; U.S. Food and Drug Administration, 2012.

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