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Suzanne M. Mahon, RN, DNSc, AOCN®, APNG, 
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Patients with advanced breast cancer are living longer and receiving multiple lines of chemotherapy; however, they eventually develop resistance to the agents. Two more agents have been approved for the treatment of breast cancer and will provide additional treatment options for such patients. Ixabepilone represents a new class of cytotoxic chemotherapy called the epothilones. Ixabepilone was approved for use as a single agent for the treatment of metastatic breast cancer resistant to taxanes, anthracyclines, and capecitabine, as well as in combination with capecitabine for disease refractory to taxanes and anthracyclines. Bevacizumab, a monoclonal antibody targeting vascular endothelial growth factor, was approved for first-line treatment of HER2-negative metastatic breast cancer in combination with paclitaxel. Understanding the efficacy, toxicity, and administration of the agents is crucial for oncology nurses to optimally educate and treat patients with advanced breast cancer.

Ixabepilone

Ixabepilone represents a novel class of cytotoxic chemotherapy, the epothilones. Epothilones exert their cytotoxic effect by binding to and stabilizing microtubules (Goodin, Kane, & Rubin, 2004), which are cellular components that have several functions crucial to cell division and growth. In a manner similar to taxanes, when bound to microtubules, epothilones disrupt their function (Goodin et al.). Evidence exists that epothilones have activity in taxane-resistant cancer cells (Goodin et al.). Other epothilones are in development, but ixabepilone is the first agent in the class to receive FDA approval. It is approved for use as a single agent for the treatment of MBC resistant to taxanes, anthracyclines, and capecitabine, as well as in combination with capecitabine for disease refractory to taxanes and anthracyclines.

At a Glance

- Metastatic breast cancer responds to multiple types of therapies, but drug resistance remains a clinical challenge.
- Ixabepilone, a first-in-class epothilone, recently was approved for use in patients with resistant breast cancer.
- Bevacizumab has been approved for use in combination with paclitaxel for upfront use in metastatic breast cancer.
Clinical Studies

In August 2007, four phase II studies of single-agent ixabepilone in MBC were published in the Journal of Clinical Oncology. Each study tested ixabepilone in a different MBC population: patients who had not received taxanes previously; those who were taxane-resistant; patients who were resistant to taxanes, anthracyclines, and capecitabine; and those who had not received therapy for MBC but had received an anthracycline as adjuvant therapy (Denduluri et al., 2007; Perez et al., 2007; Roche et al., 2007; Thomas, Tabernero, et al., 2007) (see Table 1). Ixabepilone showed activity in all of the studies, with response rates ranging from 57% in the patients without prior taxane treatment to 12% in patients who were taxane resistant.

Prior to ixabepilone, capecitabine was the only FDA-approved chemotherapy for taxane- and anthracycline-resistant breast cancer. Preclinical models showed synergy between the two agents (Lee et al., 2006). The recently published phase III study of ixabepilone with capecitabine versus capecitabine alone was conducted at 160 study sites in 22 countries and included 752 patients with MBC whose disease progressed after treatment with an anthracycline and taxane (Thomas, Gomez, et al., 2007). Most patients received an anthracycline and taxane for metastatic disease, but 8% relapsed within one year of receiving the agents in the adjuvant setting. The response rate for the combination of capecitabine and ixabepilone was significantly higher than capecitabine alone (35% versus 14%). In addition, progression-free survival was significantly increased from 4.2 months with capecitabine alone to 5.8 months for the combination (see Figure 1). In a planned subset analysis, the benefit was seen across all groups regardless of performance, estrogen receptor, or HER2 status.

Toxicity

Overall, toxicity was manageable with ixabepilone as a monotherapy. As with other cytotoxic chemotherapy, bone marrow suppression is ixabepilone’s major toxicity. Neutropenia and anemia occurred in the majority of patients across all ixabepilone studies; however, febrile neutropenia was uncommon (Perez et al., 2007). The most common nonhematologic toxicities of any grade observed in the largest of the phase II monotherapy trials of ixabepilone were neuropathy (60%), fatigue (50%), myalgia or arthralgia (49%), alopecia (48%), and nausea (42%) (Abraham, 2007). Patients who have received neurotoxic agents, such as taxanes, may be more susceptible to developing neuropathy. Ixabepilone-associated neuropathy usually is sensory and cumulative but reversible (Thomas, Tabernero, et al., 2007). It typically begins around the fourth cycle. Assessment of neuropathy signs and symptoms should be performed on all patients at each visit and noted in their charts. Common grading systems for neuropathy are shown in Table 2. Dose-adjustment guidelines for toxicity are shown in Table 3.

Liver function should be checked because patients with impaired liver function can have impaired metabolism of ixabepilone, leading to higher blood levels, which can increase the risk of toxicity. Dosage adjustments are recommended for liver dysfunction (see Table 4). In the phase III trial, adverse effects commonly seen with capecitabine, such as hand-foot syndrome, were not more common in patients who received combined capecitabine and ixabepilone (Thomas, Gomez, et al., 2007). Hematologic toxicity increased with combination therapy; however, the routine use of growth factors is not recommended (Thomas, Gomez, et al., 2007). Combination therapy is not recommended for patients with liver dysfunction of grade 2 or higher (aspartate transaminase or alanine transaminase > 2.5 × the upper limit of normal or bilirubin > 1.5 × the upper limit of normal).

Administration

The recommended starting dose of ixabepilone, as monotherapy or in combination with capecitabine, is 40 mg/m² via IV over three hours every three weeks (Bristol-Myers Squibb Company, 2007). Because polyethoxylated castor oil (Cremophor®; BASF Corporation) is used as a solvent, all patients should be premedicated one hour before administration of ixabepilone with an H1 antagonist (diphenhydramine 50 mg

![Figure 1. Effect of Ixabepilone Plus Capecitabine and Capecitabine Alone on Progression-Free Survival](image-url)

Note. Based on information from Thomas, Gomez, et al., 2007.

**Table 1. Phase II Studies of Ixabepilone in Metastatic Breast Cancer**

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PATIENT POPULATION (N)</th>
<th>DOSE</th>
<th>PR (%)</th>
<th>SD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denduluri et al., 2007</td>
<td>No previous taxane in adjuvant or metastatic setting (23)</td>
<td>6 mg/m² days 1–5 every three weeks</td>
<td>57</td>
<td>26</td>
</tr>
<tr>
<td>Perez et al., 2007</td>
<td>Anthracycline-, taxane-, and capecitabine-resistant (126)</td>
<td>40 mg/m² every three weeks</td>
<td>18.3</td>
<td>50</td>
</tr>
<tr>
<td>Roche et al., 2007</td>
<td>Previous treatment with adjuvant anthracycline (65)</td>
<td>40 mg/m² every three weeks</td>
<td>41.5</td>
<td>35</td>
</tr>
<tr>
<td>Thomas, Tabernero, et al., 2007</td>
<td>Taxane-resistant (49)</td>
<td>40 or 50 mg/m² every three weeks</td>
<td>12</td>
<td>41</td>
</tr>
</tbody>
</table>

PR—partial response; SD—stable disease
Orally or equivalent) and an H₂ antagonist (ranitidine 150–300 mg orally or equivalent) to prevent hypersensitivity reactions. If a patient experiences a hypersensitivity reaction, corticosteroids must be used as premedication with subsequent courses. Ixabepilone must be mixed with the diluent supplied with the drug and administered with lactated Ringer’s solution, not normal saline, to avoid precipitation. Nursing considerations and patient education points for ixabepilone are shown in Figure 2.

Ongoing Research With Ixabepilone

Ixabepilone is being studied in novel combinations (www.clinicaltrials.gov). Positive results in the metastatic setting have prompted the study of ixabepilone for early-stage breast cancer; therefore, neoadjuvant and adjuvant clinical trials are ongoing. For now, ixabepilone provides another option for patients with breast cancer who have progressed through frontline chemotherapy; however, ongoing research will further delineate its role in the treatment of breast cancer.

Bevacizumab

Bevacizumab is a monoclonal antibody that targets VEGF, a growth factor involved in angiogenesis. It binds to VEGF and prevents the interaction of VEGF to its receptors on the cells. Patients with breast cancer have elevated serum levels of VEGF, and breast cancer cells have a higher level of VEGF expression than normal cells. Therefore, targeting VEGF to treat breast cancer has a scientific rationale based on the biology of breast cancer (Heer et al., 2001). Although the precise mechanism by which VEGF inhibition exerts antitumor effects is not understood fully, it is thought to prevent the development of new tumor blood vessels, cause regression of existing tumor blood vessels, have some direct tumor cell effects, and decrease intratumoral fluid pressure, which may help chemotherapy penetrate the tumor (Dvorak, 2002). Previously approved for the treatment of colorectal and non-small cell lung cancers, bevacizumab has been approved for the first-line treatment of metastatic, HER2-negative breast cancer in combination with paclitaxel.

Clinical Studies

Results have been published from two phase III studies of bevacizumab for the treatment of MBC. The first was a comparison of capecitabine alone versus bevacizumab plus capecitabine in 462 patients who had received anthracyclines and taxanes (Miller et al., 2005). The response rate increased significantly in patients receiving the combination compared with patients receiving capecitabine alone (19.8% versus 9.1%). However, neither progression-free nor overall survival was increased significantly.

In the pivotal phase III study (E2100) (Miller et al., 2007), which led to the approval of bevacizumab for MBC, bevacizumab plus paclitaxel was compared with paclitaxel alone in 722 patients with breast cancer who had not received prior cytotoxic therapy for metastatic disease. In the monotherapy arm, paclitaxel alone was given at a dose of 90 mg/m² on days 1, 8, and 15 of a 28-day cycle. In the combination arm, the same dose of paclitaxel was combined with bevacizumab 10 mg/kg on days 1 and 15. Adding bevacizumab to paclitaxel significantly increased progression-free survival over paclitaxel alone (11.8 versus 5.9 months), as well as the response rate (36.9% versus 21.2%). Overall survival did not increase in the paclitaxel mono-therapy group compared with the combination paclitaxel plus bevacizumab group (26.7 versus 25.2 months) (see Figure 3). Although the study did lead to FDA approval for bevacizumab in combination with paclitaxel for MBC, the decision was not

<table>
<thead>
<tr>
<th>NEUROPATHY</th>
<th>GRADE 1</th>
<th>GRADE 2</th>
<th>GRADE 3</th>
<th>GRADE 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor</td>
<td>Asymptomatic; weakness on examination or testing only</td>
<td>Symptomatic weakness interfering with function but not interfering with activities of daily living</td>
<td>Weakness interfering with activities of daily living; bracing or assistance to walk indicated</td>
<td>Life threatening or disabling (e.g., paralysis)</td>
</tr>
<tr>
<td>Sensory</td>
<td>Asymptomatic; loss of deep tendon reflexes or paresthesia but not interfering with function</td>
<td>Sensory alteration or paresthesia interfering with function but not interfering with activities of daily living</td>
<td>Sensory alteration or paresthesia interfering with activities of daily living</td>
<td>Disabling</td>
</tr>
</tbody>
</table>

Note. Based on information from National Cancer Institute, 2006.

<table>
<thead>
<tr>
<th>TOXICITY</th>
<th>ADJUSTMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonhematologic</td>
<td></td>
</tr>
<tr>
<td>Grade 2 neuropathy (moderate) lasting ≥ 7 days</td>
<td>Decrease dose 20%</td>
</tr>
<tr>
<td>Grade 3 neuropathy (severe) lasting &lt; 7 days</td>
<td>Decrease dose 20%</td>
</tr>
<tr>
<td>Grade 3 neuropathy (severe) lasting ≥ 7 days or disabling neuropathy</td>
<td>Discontinue treatment</td>
</tr>
<tr>
<td>Any grade 3 toxicity (severe) other than neuropathy</td>
<td>Decrease dose 20%</td>
</tr>
<tr>
<td>Transient grade 3 arthralgia or myalgia or fatigue</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Grade 3 hand-foot syndrome (i.e., palmar-plantar erythrodysesthesia)</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Any grade 4 toxicity (disabling)</td>
<td>Discontinue treatment</td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
</tr>
<tr>
<td>Neutrophil &lt; 500 cells/mm³ ≥ 7 days</td>
<td>Decrease dose 20%</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>Decrease dose 20%</td>
</tr>
<tr>
<td>Platelets &lt; 25,000/mm³ or platelets &lt; 50,000/mm³ with bleeding</td>
<td>Decrease dose 20%</td>
</tr>
</tbody>
</table>

Note. Based on information from Bristol-Myers Squibb Company, 2008.
without controversy. The Oncology Drug Advisory Committee did not recommend approval, but the FDA did not follow the recommendation and granted accelerated approval (Oncologic Drugs Advisory Committee, 2007). The debate centered on the lack of overall survival benefit observed. The FDA believed, however, that significant clinical benefit existed to justify the use of bevacizumab for MBC.

**Toxicity**

Investigators did not believe that bevacizumab had a large impact on the side effects expected with paclitaxel, but grades 3 and 4 neuropathy, infection, hypertension, and fatigue were significantly increased in the combination group (Miller, 2007) (see Table 5). Also, grade 3 and 4 cerebrovascular ischemia, headache, and proteinuria in the combination group were significantly higher, but the overall incidence was low. In general, bevacizumab is well tolerated, but serious adverse events are possible. Bevacizumab can impair wound healing, cause bleeding, and induce arterial thrombosis, such as cerebral infarction or myocardial infarction. Although uncommon, serious events, such as stroke or myocardial infarction, can be devastating. Hypertension is more common, can be persistent, and should be treated with standard antihypertensive therapy, such as an angiotensin-converting enzyme inhibitor, beta blocker, diuretic, or calcium channel blocker. Guidelines for management of hypertension can be found in the Seventh Report of the Joint

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**Table 4. Dose Adjustment for Ixabepilone as Monotherapy in Patients With Hepatic Impairment**

<table>
<thead>
<tr>
<th>LEVEL OF IMPAIRMENT</th>
<th>TRANSMAMINASE AND BILIRUBIN Levels</th>
<th>IXABEPILONE (mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>AST and ALT ≤ 2.5 × ULN and ≤ 1 × ULN</td>
<td>40</td>
</tr>
<tr>
<td>Mild to moderate</td>
<td>AST or ALT ≤ 10 × ULN and ≤ 1.5 × ULN</td>
<td>32</td>
</tr>
<tr>
<td>Moderate</td>
<td>AST or ALT ≤ 10 × ULN and 1.5 × ULN ≤ 3 × ULN</td>
<td>20–30</td>
</tr>
</tbody>
</table>

* Excluding patients whose total bilirubin is elevated because of Gilbert disease

* Dosage recommendations are for first course of therapy; further decreases in subsequent courses should be based on individual tolerance.

* ALT—alanine transaminase; AST—aspartate transaminase; ULN—upper limit of normal

*Note. Based on information from Bristol-Myers Squibb Company, 2008.

**Proprietary name:** Ixempra®

**Indications:** In combination with capecitabine for the treatment of metastatic or locally advanced breast cancer resistant to an anthracycline and a taxane, or for use in patients in whom further anthracycline therapy is contraindicated; as monotherapy for treatment of metastatic or locally advanced breast cancer resistant or refractory to anthracyclines, taxanes, and capecitabine.

**Pharmacology:** Microtubule inhibitor

**Dosage:** 40 mg/m² every three weeks via IV infusion over three hours

**Most common side effects:** Peripheral sensory neuropathy, fatigue and asthenia, myalgia and arthralgia, alopecia, nausea, vomiting, stomatitis and mucositis, diarrhea, and musculoskeletal pain

**Nursing considerations**

- Premedicate with H₁ antagonist and H₂ antagonist; add corticosteroid if patient had a previous hypersensitivity reaction.
- Monitor for symptoms of neuropathy, primarily sensory, which are cumulative and usually reversible; neuropathy should be managed by dose adjustment and delays.
- Monitor for myelosuppression with peripheral blood cell counts and adjust dose as appropriate.
- Inhibitors of CYP3A4 may increase plasma concentrations of ixabepilone; reduce dose in patients on CYP3A4 inhibitors. No grapefruit, grapefruit juice, or any grapefruit product prior to treatment

**Figure 2. Nursing Considerations and Patient Education Points for Ixabepilone**


**Figure 3. Survival Analysis of Paclitaxel Plus Bevacizumab Versus Paclitaxel Alone**

*Note. Based on information from Miller et al., 2007.
National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (National Heart, Lung, and Blood Institute, 2003) Patients should be screened for hypertension, but no recommendations exist to check for heart dysfunction. It should be used with caution in patients with a history of angina or myocardial infarction, but it is not contraindicated.

Administration

The recommended dose of bevacizumab in combination with paclitaxel for MBC is 10 mg/kg every 14 days. The infusion is typically given over 90 minutes and shortened to 60 minutes then 30 minutes on subsequent infusions. However, infusions as short as 10 minutes were performed safely in a study from Memorial Sloan-Kettering Cancer Center (Reidy et al., 2007). The incidence of infusion reactions to bevacizumab is less than 3%, and severe reactions have been reported in 0.2% of patients across all studies (Genentech, Inc., 2008). Because bevacizumab is indicated for use with paclitaxel in patients with MBC, premedication with antihistamines and corticosteroids is required for prophylaxis of infusion reactions. Because bevacizumab can interfere with wound healing, it should not be given for at least 28 days after surgery (Genentech, Inc.). Some recommend waiting six weeks. In addition, bevacizumab should be stopped several weeks before any planned surgery. Although no standard recommendations exist for dose modification of bevacizumab when side effects occur, some clinical situations require that bevacizumab be suspended or discontinued (see Figure 4).

Ongoing Research With Bevacizumab

Numerous randomized studies are ongoing to help clarify the optimal use of bevacizumab in MBC. The trials will further define the place of bevacizumab in breast cancer treatment.

Conclusions

Although the treatment of breast cancer has improved dramatically, MBC continues to be a major health problem. Taxanes (paclitaxel, docetaxel, and nab-paclitaxel) and anthracyclines (doxorubicin and epirubicin) are cornerstones of breast cancer treatment; however, many patients eventually develop resistance. Consequently, research has focused on the development of new agents. The discovery of the epothilone class of drugs and the recent FDA approval of ixabepilone have been significant advances. The results of clinical trials of ixabepilone as a single agent and in combination with capecitabine were positive: Ixabepilone demonstrated a manageable safety profile similar to that of other chemotherapy agents, is capable of overcoming chemotherapy-induced resistance,

| Table 5. Treatment-Related Toxic Effects of Paclitaxel With and Without Bevacizumab |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **EFFECT** | **PACLITAXEL PLUS BEVACIZUMAB (N = 365)** | **PACLITAXEL (N = 346)** | **GRADE 3 (%)** | **GRADE 4 (%)** | **GRADE 3 (%)** | **GRADE 4 (%)** | **p** |
| Allergic reaction | 3.0 | 0.3 | 2.6 | 0.3 | NS |
| Neutropenia | – | – | 0.3 | – | NS |
| Anemia | 0.3 | – | – | – | NS |
| Thrombocytopenia | – | – | – | 0.3 | NS |
| Infection | 8.8 | 0.5 | 2.9 | – | < 0.001 |
| Fatigue | 8.8 | 0.3 | 4.6 | 0.3 | 0.04 |
| Nausea | 3.3 | – | 1.2 | – | NS |
| Sensory neuropathy | 23 | 0.5 | 17.1 | 0.6 | –0.05 |
| Hypertension | 14.5 | 0.3 | – | – | 0.02 |
| Thrombosis or embolism | 1.6 | 0.5 | 0.6 | 0.9 | NS |
| Cerebrovascular ischemia | 0.8 | 1.1 | – | – | 0.02 |
| Left ventricular dysfunction | 0.8 | – | – | 0.3 | NS |
| Hemorrhage | 0.5 | – | – | – | NS |
| Gastrointestinal perforation | 0.5 | – | – | – | NS |
| Headache | 2.2 | – | – | – | 0.008 |
| Proteinuria | 2.7 | 0.8 | – | – | < 0.001 |

NS—not significant

Note. Based on information from Miller et al., 2007.
Inset 1. Case Study

T.D. is a 54-year-old postmenopausal woman who presented in July 1998 with a mass found in her left breast during a physical examination. A mammogram showed a large, 5.2 cm, spiculated lesion. A biopsy revealed invasive ductal carcinoma, which was estrogen receptor positive, progesterone receptor positive, and HER2 negative. Her bone scan and abdominal and pelvic computed tomography scan were normal, as was her chest x-ray.

Her diagnosis was stage III infiltrating breast cancer, which was treated with neoadjuvant paclitaxel followed by cyclophosphamide, doxorubicin, and fluorouracil. She subsequently underwent a left segmental mastectomy and axillary dissection. At surgery, the tumor showed evidence of response: It was now 2.1 cm. Her lymph nodes were negative for carcinoma. Local radiation therapy was given, and she was started on tamoxifen. The patient did well during treatment but reported being fatigued.

The patient did well until June 2002, when she developed painful metastasis in the left pelvic bone and supraclavicular lymph nodes. Her performance status remained excellent.

What measures can be taken to help patients who experience fatigue?

The evidence-based literature shows that fatigue is the primary factor that worsens quality of life for all patients with breast cancer, whether in the adjuvant or metastatic setting.

At a recent conference, a group of physicians who were themselves cancer survivors said overwhelmingly that fatigue was the most disturbing side effect they experienced throughout their treatment. In fact, patients often experience fatigue for 6–12 months after completing therapy. Fatigue is one of the most important side effects to assess. In addition, nurses must educate patients about fatigue as a side effect.

Fatigue is a multifactorial symptom requiring a multidimensional approach. The National Comprehensive Cancer Network (NCCN) guidelines (NCCN, 2008) and the Oncology Nursing Society (n.d.a) Putting Evidence Into Practice® (PEP) materials are excellent resources. They present many potentially useful interventions and recommend that patients be screened for fatigue at each visit, much like assessment of vital signs. A fatigue assessment might include when and how severe fatigue is, as well as factors that trigger specific bouts of fatigue.

Fatigue assessment can serve as a guide when developing an individualized plan to help a patient cope with fatigue. Some studies have evaluated pharmacologic interventions, such as methylphenidate. However, simpler, nonpharmacologic interventions are recommended to manage fatigue, such as exercise, distraction, relaxation, energy conservation, optimization of sleep quality, and patient education (Oncology Nursing Society, n.d.a). Attention-restoring activities—walking regularly, staring out the window, looking at the clouds, watching the traffic—can be helpful during the day. Working half-days, job sharing, having someone care for children in the afternoon, napping, and maintaining an exercise regimen are other energy-conserving activities.

What are therapeutic options for this patient who has progressed to metastatic disease?

An assessment of T.D. revealed that she had no life-threatening organ involvement. She was, however, symptomatic and had pain from the left pelvic bone lesion. Chemotherapy was an option. According to the NCCN (2008) guidelines, single-agent chemotherapy would be appropriate because no rapid response is needed; most data on combination chemotherapy show that it does not prolong survival. A second hormonal agent would be appropriate as well. After the healthcare team considered the options, the patient was started on anastrozole and received local radiation to the left pelvis. Her pain was relieved, and her disease remained stable until September 2003, when two new, asymptomatic bone lesions were found.

What are the therapeutic choices now?

Although a third hormonal agent such as fulvestrant could have been given, chemotherapy was more appropriate because T.D. had stable disease on anastrozole for one year without a response. Docetaxel was given, but within six months her disease progressed into her lymph nodes. Capecitabine was given, but her nodal disease progressed and a pulmonary lesion developed after five months.

Would a clinical trial be appropriate?

Nurses play an important role in educating patients about the availability of clinical trials. In this case, T.D. asked about entering a clinical trial. She had adjuvant treatment with paclitaxel and doxorubicin. She was given two hormonal agents and received docetaxel and capecitabine as sequential, single-agent therapy for metastatic disease.

In consideration of her previous treatment, she was enrolled in August 2004 into a clinical trial with ixabepilone. During the first four months on ixabepilone, significant shrinkage of her axillary and supraclavicular nodes occurred, which stabilized until the eighth month; at that time, her disease progressed again. T.D. tolerated the ixabepilone treatment very well. She had no need for dose reductions or delays through her nine courses of ixabepilone. Her side effects included mild diarrhea, moderate fatigue, mild to moderate sensory neuropathy, and neutropenia without fever.

T.D.’s case was gratifying in that ixabepilone was clinically beneficial to a patient who was heavily pretreated. In fact, the benefit from ixabepilone lasted eight months, whereas the benefit from docetaxel and capecitabine was six and five months, respectively.

What is your approach to managing neuropathy?

The most important point is careful initial and ongoing assessment and quick, aggressive management, especially with dose reductions. Patient education also is extremely important to preserve patient safety. The Oncology Nursing Society (n.d.b) PEP card on peripheral neuropathy is a good resource.

and demonstrated activity in minimally and heavily pretreated patients with MBC. Based on the available clinical evidence, ixabepilone is a promising agent for patients with resistant MBC. Further development of the epothilone drug class and combination of such agents with other anticancer agents may play a pivotal role in treating a variety of metastatic cancers.

Targeted therapies developed to treat hormone-positive and HER2-positive breast cancer have been immensely successful. Development of monoclonal antibodies that target VEGF is a novel approach in the treatment of HER2-negative breast cancer, a focus recently strengthened by favorable results with combination bevacizumab and paclitaxel.

Side effects with ixabepilone and bevacizumab generally are manageable, especially if detailed patient teaching and assessments are performed by oncology nurses and reinforced by other healthcare professionals (see Insets 1 and 2). Effective interactions between patients and oncology nurses are vital to the overall success of the treatment program, which includes...
Inset 2. Author Commentary

Commentary 1: Ixabepilone Therapy in Metastatic Breast Cancer Treatment

Debra K. Frye, RN, BSN, OCN®, CCRP: I’ve been working in the field of breast cancer care for many years. When I started out, single-agent therapy was the primary option, and survival was usually less than a year. When combination therapy became available, the outlook for patients began to improve. Oncologists now have multiple single-agent and combination therapy regimens available that have further improved patient outcomes. The two newest approved options—ixabepilone and bevacizumab—are very exciting.

Suzanne M. Mahon, RN, DNSc, AOCN®, APNG: In terms of patient selection for ixabepilone, it can be used with capecitabine in patients who received an anthracycline and taxane. Ixabepilone alone would be indicated in patients who are refractory to all three agents—an anthracycline, a taxane, and capecitabine. This is one of the exciting things about this drug. You can treat patients with the best agents you have, including capecitabine, but if the patient has refractory disease, you can still induce a response to ixabepilone alone. It is exciting to finally have a drug in that category. There were other treatments available to patients, but the data showing results in patients with resistant disease are lower, and the response rates really have not been as good. This is a hopeful point to communicate to patients as they are going from therapy to therapy: Regimens exist that can help.

Frye: As nurses, we should be aware of the vast amount of research that is under way to determine the best ways to further integrate ixabepilone into practice. Several trials are looking into its use in combination with other drugs, including trastuzumab. More information will be available in the near future. We must be ready to accurately communicate this information to patients and nursing colleagues and learn to use these new combinations as quickly as possible.

Commentary 2: Nursing Considerations With Ixabepilone Therapy

Frances M. Palmieri, RN, MSN, OCN®, CCRP: It is important for nurses to know the premedication protocol for ixabepilone: H1 and H2 blockers are administered, not dexamethasone. Although the drug has the solvent polyethoxylated castor oil (Cremophor®, BASF Corporation), just like paclitaxel, the total dose is lower. Therefore, the incidence of hypersensitivity has been much lower. If patients experience a hypersensitivity reaction to ixabepilone, then dexamethasone or another corticosteroid is administered.

Frye: Teaching patients about the potential for ixabepilone-related neuropathy and assessing for neuropathy at regular intervals, including baseline evaluation, is important. In addition, it is important to alert the patient about potential fever and infection and the need for blood count monitoring.

Patients should be made aware of drug contraindications. Because ixabepilone is a CYP3A4 inhibitor, patients should be advised about drugs that may interact with it and affect its metabolism. Strong CYP3A4 inhibitors include drugs, such as ketoconazole, clarithromycin, and atazanavir. Patients should avoid drinking grapefruit juice because it, too, may increase plasma concentrations of ixabepilone.

If capecitabine is going to be used, the patient must be counseled about the potential for hand-foot syndrome. Because capecitabine is an oral medication, adherence to therapy must be emphasized.

Commentary 3: Nursing Considerations With Bevacizumab Therapy

Palmieri: Many patients experience an increase in blood pressure with bevacizumab. Therefore, know your patient’s baseline blood pressure. Patient education on hypertension is essential, and careful monitoring by the nurse can help keep the patient safely on therapy. The nurse also should be aware of the potential for proteinuria. When elevations occur, the drug should be discontinued until the patient’s blood pressure level returns to baseline.

Mahon: Blood pressure has been more of a concern with patients with lung cancer. Even patients without a history of significant hypertension experienced increases in blood pressure. In patients with very mild hypertension, increases occurred almost immediately.

Palmieri: One difference between patients with lung cancer and those with breast cancer is the incidence of nose bleeds. Although epistaxis was not common in patients with breast cancer, the possibility exists. Counsel patients to report a nose bleed immediately. In addition, try to get ports in patients during their first surgical events so wound healing is not a problem. Talk to patients before administering bevacizumab to make sure no surgery is planned during the treatment period.

not only response to treatment, but patient safety, adherence, and an acceptable quality of life.

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References


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