

# CONQUERING THE CANCER CARE CONTINUUM™

## Advances in Side Effect Management

Lillie D. Shockney, RN, BS, MAS

University Distinguished Service Associate Professor of Breast Cancer  
Johns Hopkins University School of Medicine, Baltimore, MD

Among the various types of treatment that a patient with cancer may undergo, chemotherapy is associated with the greatest concerns with respect to side effects. Although patients may comprehend the importance of receiving chemotherapy as a key component of their treatment plan, the fear of adverse events (AEs) is always foremost on their minds. This third issue of *Conquering the Cancer Care Continuum™* focuses on this topic, and provides insight into the critical role played by oncology pharmacists and nurses in the management of treatment-related side effects. Without the effective management of such complications as chemotherapy-induced nausea and vomiting (CINV), peripheral neuropathy, fatigue, and insomnia, a patient may decide to discontinue therapy prematurely. This could likely result in that individual not receiving the intended benefits of treatment. Such side effects do not merely disrupt a patient's quality of life (QOL), they can also result in an individual's life becoming totally derailed. For example, a patient may need to work for financial reasons while undergoing chemotherapy. If the AEs experienced during and following each treatment cycle are associated with the patient not being able to function well physically and/

or mentally, this may become a barrier to adherence.

We must also be mindful of asking patients what their life goals are and of striving on their behalf to dovetail those goals into the treatment plan. For example, if an individual is studying to become a concert pianist and his or her scheduled chemotherapy regimen includes agents that are known to induce long-term neuropathy, we would be potentially robbing that individual of important career goals. Thus, there are numerous issues to consider when selecting a combination of agents and planning for the administration of therapy, with the goal being for the patient to take the regimen as prescribed while, at the same time, having his or her side effects minimized to the best of our ability.

In this publication, several drug classifications will be discussed by an oncology pharmacist who is an expert on side effect management. An oncology nurse will also provide her perspective on the important role played by nurses in caring for patients undergoing chemotherapy. Whenever possible, we want to proactively prevent AEs from occurring. If that is not possible, then minimizing symptoms so they are manageable and do not disrupt a patient's daily routine is the next desired outcome. Educating



Lillie D. Shockney,  
RN, BS, MAS

patients on what to expect and on the management of AEs is imperative as we prepare them for each phase of treatment.

As more agents for the management of side effects transition from intravenous (IV) to oral drugs, the need for effective patient education must be recognized. We are placing the responsibility on the patient and on his or her family members to take oral medications as prescribed. This may be difficult for some individuals if they have memory problems, an unusual work schedule, or other barriers that might result in them not receiving the medications at the right time in the right dosage and in the right sequence. For this reason, nurses must be proactive and follow up with their patients by phone, rather than waiting for them to call the clinic or show up for their next appointment.

Novel agents are being developed for the management of CINV, and it is important for oncology specialists to remain informed about what is coming down the research pike. In the last 2 to 3 decades, we have witnessed great improvements in the development and standardization of US Food and Drug Administration–approved drugs that have improved QOL among patients undergoing chemotherapy. It is very important to share these advances with our patients so they can make informed decisions regarding their care.

One issue remains, however, and for an ironic rea-


son. Third-party payment for IV medications remains a covered service. However, some very effective antiemetic agents are administered orally. In certain cases, these medications are not covered by insurance because they *are* oral medications. We need to push this issue from a regulatory perspective. It is very advantageous to have patients empowered to manage their side effects at home, and this can often be done safely with the use of oral drugs designed for that purpose. If the out-of-pocket expenses exceed what is financially realistic for a patient to handle, however, oncologists must then default to having that patient continue to visit an oncology facility and receive older IV medications. This is just not logical. I am a believer in having a patient’s voice heard when changes in regulations are needed. When a pharmaceutical company speaks, there is a high probability that its voice is not heard, because this would probably be considered a conflict of interest. When an oncology specialist speaks, there also may be an assumption that this in some way benefits the cancer care team. When a patient describes his or her experience, however, people listen.

It is my hope that the following articles will provide useful information that you can use to advocate for your patients, and provide them with the tools they need to reap the benefits of treatment while maintaining QOL throughout the continuum of care. ■


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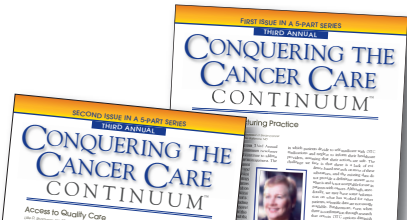
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## Side Effect Management: A Nurse's Perspective

Beth Fairman, PhD, MSN, APRN-BC, AOCN  
Nurse Practitioner, Cleveland Clinic Taussig Cancer Institute  
Cleveland, OH

It is inevitable that patients with cancer will experience some side effects associated with treatment. Recommendations for managing and minimizing these complications are critical to patients' well-being and can impact overall clinical outcomes. Adherence to therapy (or the ability to remain on treatment as recommended) is negatively affected when cancer symptoms and adverse events (AEs) are inappropriately managed. Although it is assumed that cancer is a devastating diagnosis and patients will adhere to therapy despite side effects, some patients may select quality of life (QOL) over highly toxic therapies. Lack of adherence to treatment is an unfortunate consequence of ineffective AE management. Side effects related to chemotherapy will often vary among patients with hematologic and solid tumor cancers. However, common AEs associated with the use of many chemotherapeutic regimens include fatigue, insomnia, neuropathy, and pain.<sup>1</sup>

Cancer-related fatigue (CRF) affects 60% to 90% of patients with cancer.<sup>1</sup> It is very rare to encounter an individual undergoing chemotherapy who does not complain of this condition. Although the etiology is poorly understood, fatigue negatively impacts the QOL of most patients with cancer. In addition, CRF can impair a person's ability to perform activities of daily living (eg, hygiene, preparing or shopping for food) and limit his or her employment. CRF can affect patients both physically and psychologically, which may lead to depression.<sup>2</sup>

The multifactorial and complex nature of fatigue demands comprehensive management of chronic anemia and pain, physical deconditioning, emotional stress, depression, and sleep disturbances.<sup>3</sup> Nurses play a key role in screening patients to determine modifiable causes of fatigue and implementing interventions to improve health outcomes (Figure).<sup>4,5</sup>

Guidelines on fatigue from the National Comprehensive Cancer Network<sup>5</sup> suggest that central nervous system stimulants may be used for the treatment of moderate to severe fatigue, but conflicting evidence

exists.<sup>6-8</sup> Nonpharmacologic treatments such as rest (but not too much rest during the day), adequate nutrition, and exercise remain reasonable recommendations for patients with CRF, along with dose modification of the offending drug when possible.

Insomnia, or difficulty sleeping, is often multifactorial and can be associated with cancer pain, depression, or corticosteroid use for the treatment of hematologic cancers. Poor sleep and poor sleep quality negatively impact a patient's QOL.<sup>9</sup> Benzodiazepines and nonbenzodiazepine hypnotics are commonly administered in combination with nonpharmacologic management, such as sleep hygiene (avoidance of caffeine and exercise before bedtime, regular exercise routine) and the avoidance of daytime naps. The

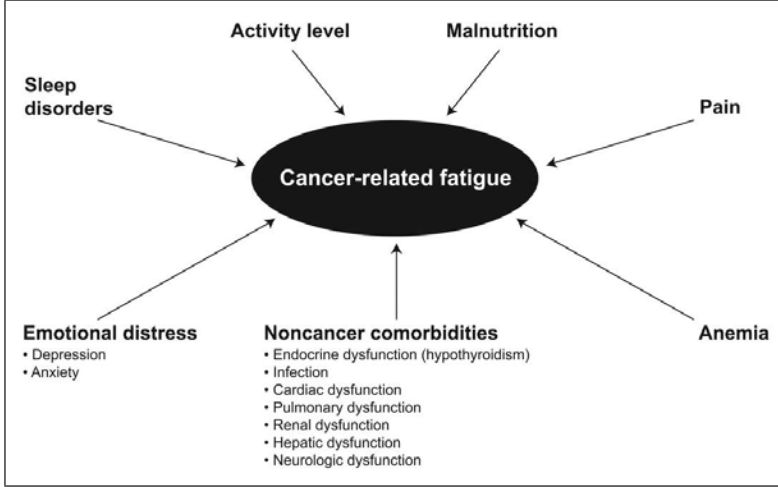
use of cognitive behavioral therapy and relaxation therapy has become more common in recent years, and can address insomnia with a variety of nonpharmacologic approaches.<sup>9</sup> Ensuring that a patient with insomnia does not have sleep apnea or another potentially serious health condition is an important nursing consideration.

Peripheral neuropathy (PN) is characterized by numbness and tingling or pain in 1 or more extremities in patients with cancer.<sup>1,10</sup> Damage to the peripheral nerves from chemotherapy or from the disease itself can prevent an individual from successfully receiving treatment. Although no known preventive strategy exists for PN, the Oncology Nursing Society has created guidelines for the management of this condition.<sup>10</sup> Exercise seems to be an effective nonpharmacologic intervention, possibly by stimulating oxygen and blood flow to nerve endings to help with regeneration of damaged nerve fibers from a variety of etiologies.<sup>11</sup> Other nonpharmacologic strategies such as the use of glutamine have also been studied, with varied results.<sup>12-14</sup> To date, the only pharmacologic agent shown to improve painful PN in patients receiving chemotherapy is a serotonin-norepinephrine reuptake inhibitor antidepressant.<sup>15</sup> Additional research is ongoing and targets the investigation of genetic factors that predispose an individual to develop neuropathy.



Beth Fairman, PhD(c),  
MSN, APRN-BC, AOCN

Figure. Treatable contributing factors for cancer-related fatigue.<sup>4,5</sup>



Many patients with cancer experience pain at some point during the course of their disease. Pain management continues to be a major issue among cancer survivors. The World Health Organization pain ladder has been used for years to help clinicians manage pain in their patients.<sup>16</sup> However, because pain can be neuropathic (affecting nerves) or nociceptive (affecting pain receptors) and is often multifactorial in nature, an accurate diagnosis of pain etiology is critical to determine proper treatment. Opioids are effective for the management of pain (once a good pain history has been obtained), but nonpharmacologic management of pain with hypnosis, acupuncture, and behavioral therapy has also been studied and can be effective in some patients.<sup>17,18</sup>

Nurses play a vital role in caring for patients and are important members of the treatment team. It is important for all nurses, regardless of whether they are able to prescribe medications, to be aware of current side effect management strategies. Understanding and implementing these strategies can benefit patients and improve outcomes. ■

References

1. Pachman DR, Barton DL, Swetz KM, Loprinzi CL. Troublesome symptoms in cancer survivors: fatigue, insomnia, neuropathy, and pain. *J Clin Oncol*. 2012;30:3687-3696.
2. Berger AM, Abernethy AP, Atkinson A, et al. Cancer-related fatigue. *J Natl Compr Canc Netw*. 2010;8:904-931.
3. Coleman EA, Goodwin JA, Coon SK, et al. Fatigue, sleep, pain, mood and performance status in patients with multiple myeloma. *Cancer Nurs*. 2011;34:219-227.
4. Carroll JK, Kohli S, Mustian KM, et al. Pharmacologic treatment of cancer-related fatigue. *Oncologist*. 2007;12(suppl 1):43-51.
5. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cancer-Related Fatigue*. Version 1.2014. [https://www.nccn.org/store/login/login.aspx?ReturnURL=http://www.nccn.org/professionals/physician\\_gls/pdf/fatigue.pdf](https://www.nccn.org/store/login/login.aspx?ReturnURL=http://www.nccn.org/professionals/physician_gls/pdf/fatigue.pdf). Accessed October 17, 2014.
6. Spathis A, Fife K, Blackhall F, et al. Modafinil for the treatment of fatigue in lung cancer: results of a placebo-controlled, double-blind, randomized trial. *J Clin Oncol*. 2014;32:1882-1888.
7. Hovey E, de Souza P, Marx G, et al; MOTIF Investigators. Phase III, randomized, double-blind, placebo-controlled study of modafinil for fatigue in patients treated with docetaxel-based chemotherapy. *Support Care Cancer*. 2014;22:1233-1242.
8. Ruddy KJ, Barton D, Loprinzi CL. Laying to rest psychostimulants for cancer-related fatigue? *J Clin Oncol*. 2014;32:1865-1867.
9. Dickerson SS, Connors LM, Fayad A, Dean GE. Sleep-wake disturbances in cancer patients: narrative review of literature focusing on improving quality of life outcomes. *Nat Sci Sleep*. 2014;6:85-100.
10. Oncology Nursing Society; Visovsky C, Collins ML. Peripheral neuropathy; 2009. <https://www.ons.org/practice-resources/pep/peripheral-neuropathy>. Accessed October 7, 2014.
11. Dobson JL, McMillan J, Li L. Benefits of exercise intervention in reducing neuropathic pain. *Front Cell Neurosci*. 2014;8:102.
12. Savarese DMF, Savy G, Vahdat L, Wischmeyer PE, Corey B. Prevention of chemotherapy and radiation toxicity with glutamine. *Cancer Treat Rev*. 2003;29:501-513.
13. Stubblefield MD, Vahdat LT, Balmaceda CM, Troxel AB, Hesdorffer CS, Gooch CL. Glutamine as a neuroprotective agent in high-dose paclitaxel-induced peripheral neuropathy: a clinical and electrophysiologic study. *Clin Oncol (R Coll Radiol)*. 2005;17:271-276.
14. Wang W-S, Lin J-K, Lin T-C, et al. Oral glutamine is effective for preventing oxaliplatin-induced neuropathy in colorectal cancer patients. *Oncologist*. 2007;12:312-319.
15. Smith EML, Pang H, Cirrincione C, et al; the Alliance for Clinical Trials in Oncology. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial. *JAMA*. 2013;309:1359-1367.
16. World Health Organization. Cancer pain relief and palliative care: report of a WHO Expert Committee. World Health Organization Technical Report Series 804. Geneva, Switzerland: World Health Organization; 1990.
17. Pachman DR, Watson JC, Loprinzi CL. Therapeutic strategies for cancer treatment related peripheral neuropathies. *Curr Treat Options Oncol*. 2014 Aug 14 [Epub ahead of print].
18. Kravits K. Hypnosis: adjunct therapy for cancer pain management. *J Adv Pract Oncol*. 2013;4:83-88.



## The Management of Adverse Events: A Pharmacist's Perspective

Steve Stricker, PharmD, MS, BCOP

Assistant Professor of Pharmacy Practice

Samford University McWhorter School of Pharmacy, Birmingham, AL

As an oncology pharmacist in an ambulatory cancer clinic, in the course of a typical week, it is not unusual for me to counsel 25 to 30 new patients on chemotherapy regimens that they are about to receive (paying particular attention to adverse events [AEs]), and to be directly involved in the monitoring and management of countless other patients who present with side effects associated with their treatments. This is an area of practice in which a multidisciplinary approach, comprising physicians, nurses, and pharmacists, will hopefully ensure improved quality of life (QOL) for our patients while offering an excellent opportunity for collaboration with our healthcare partners. To provide high-quality supportive care to patients, it is essential that we always consider new US Food and Drug Administration (FDA)-approved treatment options and commercially available drugs indicated for other disease states, and simultaneously review the evidence supporting the use of novel agents that may reach our clinics in the months or years to come.

One of my major interests is the management of chemotherapy-induced nausea and vomiting (CINV). I am often surprised by the number of patients who will ask about this complication, rather than about their prognosis, when they first learn they will require chemotherapy for their cancer. A well-known stigma is associated with CINV, and such concerns are not without merit. Lindley and colleagues published a seminal paper on this topic in 1992, in which they evaluated the impact of CINV on functional activities and QOL in patients undergoing chemotherapy.<sup>1</sup> The results, not unexpectedly, revealed that whereas the presence of nausea compromises a patient's QOL, vomiting was consistently more bothersome.<sup>1</sup> For patients and their families, this often led to additional financial costs associated with the purchase of special foods and over-the-counter medications that were not prescribed by their oncologist.



Steve Stricker,  
PharmD, MS, BCOP

Although the Lindley trial is now more than 20 years old, to date, no other study has conducted such an extensive evaluation of the impact of CINV on QOL in patients with cancer. Even with the availability of many new agents (and entirely new classes of drugs) that have been approved for CINV since 1992, we as oncology providers still find ourselves struggling with the management of symptoms. Despite the fact that nausea has been so clearly established as a cause of reduced QOL, it is often not a measured end point in CINV clinical trials. Many commentaries point to this as a deficiency that must be corrected in future studies.

Two separate classes of drugs have contributed to some of the greatest advances in recent years with regard to CINV management. First, data support the use of certain atypical antipsychotic agents for the treatment of CINV, as mechanistically, these drugs can interact with important mediators of the CINV process, including dopamine, serotonin (5-HT<sub>3</sub>) receptor antag-

**The results, not unexpectedly, revealed that whereas the presence of nausea compromises a patient's QOL, vomiting was consistently more bothersome.**

onists (RAs), and histamine receptors. Although these agents have historically been used for their antipsychotic properties and have been associated with weight gain, their use as adjunctive therapy in this specific patient population is often reported to be beneficial (without weight gain) and is recommended by the National Comprehensive Cancer Network Clinical Practice Guidelines on Antiemesis.<sup>2</sup>

The second class of drugs that has proved to be ben-

eficial in recent clinical trials is the neurokinin-1 (NK-1) RA. Although several novel agents in this family have been in development over the past 5 years, 2 unique chemical entities are steadily gaining ground toward FDA approval. Data presented at the 2013 and 2014 American Society of Clinical Oncology (ASCO) annual meetings detail results of trials evaluating a novel NK-1 RA in a fixed-dose combination with a 5-HT<sub>3</sub> RA in a single oral dosage formulation in patients receiving moderate to highly emetogenic chemotherapy.<sup>3,4</sup> Given the significantly extended half-life of this novel NK-1 RA compared with the currently approved agent in this class, this combination therapy has shown benefit, particularly in the setting of delayed CINV. An additional novel NK-1 RA with an estimated half-life of 180 hours, used in combination with a corticosteroid and a 5-HT<sub>3</sub> RA in patients receiving highly emetogenic chemotherapy, also demonstrated a statistically significant benefit in the delayed CINV setting.<sup>5</sup> Questions remain, however, about the effectiveness of these new agents, compared with current standards of care, for the management of nausea.

If approved by the FDA, these therapies will offer practitioners additional treatment options for the management of patients with clinically significant CINV. More specifically, the use of new oral antiemetics with extended half-lives should reduce patients' need for multiple daily dosing of 5-HT<sub>3</sub> RAs, while offering benefit in the setting of delayed CINV. With multiple studies demonstrating that adherence to oral therapies in the setting of cancer management (both chemotherapy and supportive care) is approximately 50%,<sup>6-9</sup> these agents may be of particular use in this setting because they require fewer total doses. Unfortunately, because payment models for intravenous (IV) versus oral medications vary, it may remain easier (and less expensive) for some patients and for some practices to rely on IV antiemetics to ensure patients' maximum access to high-quality, evidence-based care. These are but 2 of the controversies and challenges associated with the clinical use of IV versus oral medications in oncology practice.

In addition to CINV, as an oncology pharmacist, I am routinely asked to manage many other treatment-related complications for which there are currently no FDA-approved treatments that can significantly improve QOL. Each year, I carefully study the ASCO abstracts and the latest clinical trial results in the hope of learning about advancements in the man-

agement of palmar-plantar erythrodysesthesia (hand-foot syndrome) and neuropathies associated with so many chemotherapy drugs. It is unfortunate that despite much effort to improve both of these conditions, to date, little success has been demonstrated. As a result, anecdotal remedies and nonpharmacologic approaches are often the best that we can recommend for our patients.

Overall, side effect management is a significant part of my job as an oncology pharmacist. To understand, recognize, and associate the AEs a patient is experiencing with the causative agent is, at times, a difficult task. Identifying and recommending an appropriate treatment for a particular side effect or for the prevention of symptoms in subsequent cycles of chemotherapy is equally challenging. Thus, a multidisciplinary approach to the management of patients with cancer is not only highly recommended, but is absolutely necessary to ensure that patients have the best possible access to high-quality care. ■

## References

- Lindley CM, Hirsch JD, O'Neill CV, Transau MC, Gilbert CS, Osterhaus JT. Quality of life consequences of chemotherapy-induced emesis. *Qual Life Res.* 1992;1:331-340.
- National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)*. Antiemesis. Version 2.2014. [www.nccn.org/professionals/physician\\_gls/pdf/antiemesis.pdf](http://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf). [www.nccn.org](http://www.nccn.org). Accessed October 9, 2014.
- Aapro MS, Karthaus M, Schwartzberg LS, et al. Phase 3 study of NEPA, a fixed-dose combination of netupitant and palonosetron, for prevention of chemotherapy-induced nausea and vomiting during repeated moderately emetogenic chemotherapy (MEC) cycles. *J Clin Oncol (ASCO Annual Meeting Abstracts)*. 2014;32(suppl 5). Abstract 9502.
- Hesketh PJ, Rossi G, Rizzi G, et al. Efficacy of NEPA, a novel combination of netupitant (NETU) and palonosetron (PALO) for the prevention of chemotherapy-induced nausea and vomiting (CINV) following highly emetogenic chemotherapy (HEC). *J Clin Oncol (ASCO Annual Meeting Abstracts)*. 2013;31(suppl). Abstract 9512.
- Rapoport BL, Poma A, Hedley ML, Martell RE, Navari RM. Phase 3 trial results for rolapitant, a novel NK-1 receptor antagonist, in the prevention of chemotherapy-induced nausea and vomiting (CINV) in subjects receiving highly emetogenic chemotherapy (HEC). *J Clin Oncol (ASCO Annual Meeting Abstracts)*. 2014;32(suppl 5). Abstract 9638.
- Partridge AH, Wang PS, Winer EP, Avorn J. Nonadherence to adjuvant tamoxifen therapy in women with primary breast cancer. *J Clin Oncol.* 2003;21:602-606.
- Fallowfield L, Atkins L, Catt S, et al. Patients' preference for administration of endocrine treatments by injection or tablets: results from a study of women with breast cancer. *Ann Oncol.* 2006;17:205-210.
- Lebovits AH, Strain JJ, Schleifer SJ, Tanka JS, Bhardwaj S, Messe MR. Patient noncompliance with self-administered chemotherapy. *Cancer.* 1990;65:17-22.
- Festa RS, Tamaroff MH, Chasalow F, Lanzkowsky P. Therapeutic adherence to oral medication regimens by adolescents with cancer. I. Laboratory assessment. *J Pediatr.* 1992;120:807-811.



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