



A CME On-Demand Webcast

From Science to Practice: Managing CINV and Pain in Breast Cancer Patients

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Syllabus

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Introduction

Chemotherapy-induced nausea and vomiting (CINV) and cancer- and treatment-related pain remain significant obstacles to the successful treatment of cancer patients. Not only do these events seriously impact patients' quality of life, but they may also result in reduced compliance with cancer treatment regimens, thereby jeopardizing overall patient outcomes. Approximately 70% to 80% of all patients receiving chemotherapy experience CINV,¹ and more than three quarters of cancer patients experience chronic pain during the course of their disease.² Unresolved CINV may lead to a variety of adverse systemic effects, including metabolic disorders, dehydration, loss of appetite, nutritional depletion, esophageal tears, and reopening of surgical wounds,³ which further impair patients' recovery. The consequences of unrelieved pain are equally debilitating and demoralizing.

Managing CINV and pain in cancer patients is a complex task requiring an understanding of the mechanisms of action of the various agents available and the ability to tailor combination regimens for individual patients. We hope you will join our expert panel for *From Science to Practice: Managing CINV and Pain in Breast Cancer Patients*, a webcast discussion of current and emerging antiemetic and pain medications used in the control of CINV and pain in breast cancer patients. The program will review the issues involved in preventing/treating acute, delayed, breakthrough, and anticipatory CINV and cancer-related pain and will explore the use of traditional and novel products for managing these events through case presentations. This promises to be an informative and valuable webcast.

References

1. Wisner W, Berger A. Practical management of chemotherapy-induced nausea and vomiting. *Oncology*. 2005;19:637-645.
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3. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Antiemesis. Version 1. 2007.

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Projects In Knowledge requires that faculty disclose any reference(s) to unlabeled or unapproved uses of drugs or devices as part of their presentations. The audience is advised that this CME activity will contain such discussion.

| Generic | Trade Names |
|-----------------------------------|----------------------------------|
| Acetaminophen | Anacin® Tylenol® Excedrin® |
| Alizapride | — |
| Aprepitant | Emend® |
| Bevacizumab | Avastin® |
| Cannabidiol/THC (investigational) | Sativex® |
| Capecitabine | Xeloda® |
| Capsaicin | Capsagel® |
| Carboplatin | Paraplatin® |
| Chlorpromazine | Thorazine® |
| Cisplatin | Platinol®-AQ |
| Cyclophosphamide | Cytosan® |
| Dexamethasone | Decadron® Dexone® |
| Domperidone | Motillium™ |
| Doxorubicin | Adriamycin® Doxil® Rubex® |
| Dronabinol (investigational) | Marinol® |
| Gabapentin | Neurontin® |
| Granisetron | Kytril® |
| Haloperidol | Haldol® |
| Levonantrodol | Nantrodolum |
| Lidocaine | Xylocaine® Lidoderm® |
| Lorazepam | Ativan® |
| Metoclopramide | Reglan® |
| Nabilone (investigational) | Cesamet® |
| Olanzapine | Zyprexa® Zyprexa Zydis® |
| Ondansetron | Zofran® |
| Oxycodone | Percocet® |
| Paclitaxel | Taxol® |
| Palonosetron | Aloxi® |
| Prochlorperazine | Compazine® |
| Quetiapine | Seroquel® |
| Sertralene | Zoloft® |
| Tamoxifen | Nolvadex® |
| Thiethylperazine | Torecan® |
| Trastuzumab | Herceptin® |
| Vinorelbine | Navelbine® |

Target Audience

This CME activity is designed for clinicians involved in the treatment of breast cancer patients.

Activity Goal

The goal of this activity is to provide clinicians involved in the treatment of breast cancer patients with state-of-the-science information on the management of CINV and pain.

Learning Objectives

- By evaluating the mechanisms of action of adjuvant antiemetics and other emerging agents, employ overall management strategies for specific patients requiring antiemetic therapy in the management of CINV to improve compliance with therapy.
- Evaluate the data suggesting a potential role of adjuvant cannabinoids in the future in relieving pain in breast cancer patients with difficult-to-control symptoms to improve patient quality of life.

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Faculty Roster

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William J. Gradishar, MD, FACP, received his medical degree from the University of Illinois, Abraham Lincoln School of Medicine, in Chicago, and completed a residency in internal medicine at Michael Reese Hospital and a fellowship in hematology/oncology at the University of Chicago. His affiliation with Northwestern University spans 17 years: currently he is Professor of Medicine at the Feinberg School of Medicine, as well as Director, Breast Medical Oncology, Multidisciplinary Breast Cancer Program; Director, Hematology-Medical Fellowship Training Program; and Associate Director, Lynn Sage Breast Program. Dr. Gradishar also serves on the editorial boards of numerous journals, including *Oncology*, *Current Treatment Options in Oncology*, *Clinical Breast Cancer*, and *Clinical Cancer Research*, and is a reviewer for *JAMA*, *Journal of Clinical Oncology*, *Lancet*, *European Journal of Cancer*, and other journals. He also participates in a variety of professional and scientific committees, including the Breast Cancer Core Committee (Eastern Cooperative Oncology Group), Breast Cancer Practice Guidelines Task Force (National Comprehensive Cancer Network), and Scientific Advisory Board (Breast Cancer International Research Group).

FACULTY

Kristen L. Fessele, RN, MSN, APN-C, AOCN

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Kristen L. Fessele, RN, MSN, APN-C, AOCN, is Associate Director, Office of Human Research Services, at The Cancer Institute of New Jersey, New Brunswick, New Jersey, where she is responsible for the oversight and management of clinical research activities. Prior to her current position, she was an oncology nurse practitioner, providing direct care to medical oncology patients on the breast cancer and phase I developmental therapeutics study services, and she continues to serve as an oncology nurse practitioner in the Breast Cancer Survivorship Program. Ms. Fessele received her RN degree from Northeastern University, Boston, Massachusetts, an MSN with a specialization in adult oncology from the University of Pennsylvania, Philadelphia, Pennsylvania, and certification in pain management from the University of Southern Indiana, Evansville, Indiana. She has published in several professional journals, including *Oncology Nursing Forum*, *Seminars in Oncology Nursing*, and *Clinical Journal of Oncology Nursing*, and has lectured extensively on the care of oncology patients.

Judith A. Luce, MD

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Judith A. Luce, MD, is Clinical Professor of Medicine at the University of California, San Francisco (UCSF), and Director of Oncology Services at San Francisco General Hospital. After receiving her medical degree from UCSF, she completed a residency in

internal medicine and a fellowship in hematology, both at the University of Colorado in Denver, and a fellowship in oncology at the University of Washington in Seattle. Dr. Luce has a long history of community service in association with a variety of cancer organizations and presently serves on committees at San Francisco General Hospital, UCSF, and the San Francisco Department of Public Health. Her research has been widely published and includes several recent articles on chemotherapy-induced nausea and vomiting in breast cancer patients. Currently, she is the principal investigator on a multi-institution trial of tamoxifen and raloxifene for breast cancer prevention and co-investigator on several additional studies in the field.

Vincent Maida, MD

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Vincent Maida, MD, received his medical degree from the University of Toronto in Ontario, Canada, and is a board certified specialist in palliative medicine. He is Founding Medical Director of the Centre for Palliative Care, William Osler Health

Centre, Etobicoke General Hospital, in Toronto and currently serves as Chief of Palliative Medicine there. In addition to his work at the Centre, Dr. Maida is Assistant Professor and Ian Anderson Fellow in Palliative Medicine and End of Life Care at the University of Toronto. He has published several articles on palliative care in peer-reviewed journals and continues to conduct research in this area. His present studies focus on wound management and late-stage intervention in advanced medical illness, the relationship between death acceptance and quality of life, and the role of cannabinoids in pain and symptom management. Dr. Maida has received numerous awards for his contributions to the development of palliative care.

Looking at Breakthrough Nausea/Vomiting and Cancer-Related Pain—The Cannabinoid Experience

Vincent Maida, MD

Chemotherapy-induced nausea and vomiting (CINV) and cancer-related pain exact a heavy toll on patients with cancer. Approximately 70% to 80% of chemotherapy patients experience nausea and/or vomiting, and more than three quarters of cancer patients suffer from chronic pain at some point in the course of their disease. In addition to having a significant impact on patients' quality of life, CINV and chronic pain can result in serious physiologic and functional decrements and may lead to disruption of/noncompliance with treatment. Breast cancer regimens differ substantially in their emetic potential, with cyclophosphamide and doxorubicin being among those most likely to induce nausea and vomiting. Whereas behavioral approaches have traditionally been used to manage anticipatory CINV, acute and delayed CINV require pharmacologic treatment, traditionally with dopaminergic receptor antagonists or serotonergic receptor antagonists. Despite the availability of numerous antiemetic agents that improve outcomes, CINV persists in many patients.

Because the antiemetic mechanism of action of cannabinoids differs from that of dopaminergic or serotonergic receptor antagonists, cannabinoids may provide effective antiemetic effects in patients who have an inadequate response to conventional therapy or who experience side effects with traditional agents. In an analysis of 30 studies comparing cannabinoids with

placebo or active control (prochlorperazine, metoclopramide, chlorpromazine, thiethylperazine, haloperidol, domperidone, or alizapride), cannabinoids resulted in greater control of both nausea and vomiting and were preferred by patients. Moreover, cannabinoids are showing significant promise in the management of anticipatory and delayed CINV.

Pain in cancer patients can be iatrogenic (as in post-mastectomy syndrome or chemotherapy-induced peripheral neuropathy), the result of bone metastases, or neuropathic. Cancer pain is traditionally treated with analgesics (opioids, TCAs, NSAIDs, etc.), bisphosphonates, chemotherapy (to reduce tumor size), hormonal therapy, and/or radiopharmaceuticals/radiotherapy. Unfortunately, neuropathic pain is often refractory or only partially responsive to common analgesics. In patients in whom traditional pain medications are inadequate, cannabinoids may provide a useful alternative. In clinical trials, cannabinoids proved significantly more effective than placebo in patients with chronic back pain and in those with neuropathic and multiple-sclerosis-related pain. Thus, used in conjunction with conventional agents, cannabinoids can both significantly improve control of CINV and ameliorate pain in cancer patients, thereby providing a valuable addition to overall treatment strategies.

Case Study: Breakthrough CINV with Anthracycline-Based Therapy

William J. Gradishar, MD, FACP

This case is illustrative of the breakthrough chemotherapy-induced nausea and vomiting (CINV) that can occur with standard first-line chemotherapy for breast cancer. The patient was diagnosed with ER/PR/HER2-negative, node-negative infiltrating ductal carcinoma, for which she received lumpectomy and radiation, followed by chemotherapy with doxorubicin and cyclophosphamide (AC). Although most physicians consider the AC regimen to be well tolerated, it is actually associated with a moderate risk of emesis, with approximately half of the patients receiving the regimen experiencing nausea/vomiting on days 2 and

3 following treatment. In this patient's case, breakthrough CINV occurred with the AC regimen despite antiemetic prophylaxis given according to the National Comprehensive Cancer Network (NCCN) guidelines. In managing breakthrough CINV, additional agents should be from a different drug class than initial therapy, with possible options including dopamine antagonists, metoclopramide, butyrophenones, cannabinoids, corticosteroids, or agents such as lorazepam. In this case, dexamethasone and lorazepam were added to the patient's antiemetic regimen.

Case Study: Anticipatory CINV and Opioid-Refractory Pain

Judith A. Luce, MD

This case describes the challenges in treating recurrent breast cancer in a patient suffering from severe pain from bone metastases and anticipatory and delayed chemotherapy-induced nausea and vomiting (CINV). Despite various combinations of nonsteroidal anti-inflammatory drugs, short- and long-acting opioids, antidepressants, and anti-anxiety agents, the patient continued to suffer from demoralizing bone pain. In addition, opioid-related nausea contributed to her virtually constant CINV, resulting in her becoming further discouraged, depressed, and noncompliant with her chemotherapy and bevacizumab regimen. In this

patient's case, a variety of physiologic and psychological/emotional factors—including nausea, pain, expectations/past history of CINV, fear, fatigue, anxiety, and depression—interacted to increase anticipatory nausea and pain. This suggested that a multidimensional approach would be necessary to manage these effects, reverse her poor compliance, and improve her quality of life. The addition of a cannabinoid, which provides both antipain and anti-CINV benefits, along with patient education/coaching, and acupuncture/massage to her antiemetic/pain regimen may provide better nausea and pain management options for this patient.

Case Study: Noncompliance as a Result of CINV and Pain

Kristen Fessele, RN, MSN, APN-C, AOCN

This case illustrates the benefit of cannabinoids in managing chemotherapy-induced nausea/vomiting and opioid-induced sedation in a patient with metastatic breast cancer. The patient experienced anticipatory vomiting and postchemotherapy nausea when initially treated with an anthracycline-based regimen for infiltrating ductal carcinoma 5 years earlier. At that time, she also developed herpes zoster and continues to experience poorly controlled postherpetic neuralgia. Seven months ago, she relapsed with a solitary pulmonary metastasis, for which she has been receiving paclitaxel, cisplatin, and trastuzumab. Her disease has responded to treatment with a 75% reduction in tumor size. However, she suffers from poorly controlled postchemotherapy nausea despite antiemetic therapy with dexamethasone, ondansetron, and prochlorperazine, and her postherpetic neuralgia pain has increased in frequency and intensity. The use of oxycodone, lidocaine, and gabapentin has proven ineffective in controlling her pain and she finds the sedating effects of opioids and gabapentin to be incapacitating. Fear of nausea/vomiting has led the

patient to miss treatment appointments, placing her disease response in jeopardy.

In an effort to achieve more reliable control of nausea and vomiting and gain more effective relief from her pain, a trial of a cannabinoid adjuvant, nabilone, was initiated. Cannabinoids (nabilone, dronabinol) are approved for use in controlling nausea and vomiting that has not responded adequately to conventional antiemetic treatments, and early results from clinical trials indicate that they may also be beneficial in relieving neuropathic pain and spasticity associated with multiple sclerosis and diabetic peripheral neuropathy. In this patient, nabilone resulted in improved nausea control, elimination of vomiting, and improvement in overall symptom burden. Nabilone should be used with caution in older patients, those with current or previous psychiatric disorders, and those at risk for tachycardia or orthostatic hypotension. However, in appropriate candidates, it can be a helpful adjunct to standard antiemetic regimens and to opioids for pain control.

Suggested Readings

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Berlach DM, Yorum S, Ware MA. Experience with the synthetic cannabinoid nabilone in chronic noncancer pain. *Pain Med*. 2006;7:25-29.

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