

# Educational Program Abstracts

## Fourth Annual Chicago Supportive Oncology Conference

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### Testosterone Replacement and Sexuality Issues in Breast Cancer

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Studies have shown that decreased sexual health is a prevalent issue that impacts the quality of life of women with breast cancer. In one study, women with breast cancer who were between 5 and 10 years post diagnosis reported significantly decreased sexual activity since their diagnosis. Another study, sponsored by the American Cancer Society, found that adult cancer survivors reported several problems 1 year after diagnosis relating to sexual health, including a decreased ability to have intercourse, discomfort with one's physical appearance, and problems communicating with a spouse or partner. Use of chemotherapy can result in menopause and estrogen deficiency. Estrogen is linked to vaginal tissue health, and deficiencies in this hormone can result in vaginal dryness and dyspareunia. However, the method in which cancer treatment impacts androgen levels is unknown. Based on data mostly related to men, testosterone can impact energy, mood, and sex drive. A clear relationship between testosterone and these variables has never been shown in women. Whether women experience testosterone deficiency and whether testosterone can impact sexual health or contribute to the risk of breast cancer are still open to debate. This session will provide emerging data regarding the breadth of sexual health issues in female cancer survivors and the impact of cancer treatment on androgen concentrations. Results of a placebo-controlled trial evaluating transdermal testosterone to improve libido in cancer survivors will be reviewed, and safety considerations will be discussed. There is a need to learn more about the role of testosterone and the physiology of sexual health in women with breast cancer to better address the complications of the disease and its treatment.

### Aromatase Inhibitor-Associated Arthralgia

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Aromatase inhibitors (AIs) are valuable adjuvant endocrine treatments for postmenopausal women with estrogen receptor-positive breast cancer. With the increasing use of these agents, a new appreciation for their side effects has emerged. Among the common side effects of AI therapy is a musculoskeletal disorder that includes arthralgias, a condition patients typically describe as an onset of joint stiffness or achiness, particularly in the hands, arms, knees, and back. The precise etiology for such symptoms is not known, though it is thought to relate to the profound estrogen deprivation seen with AI therapy. The data on interventions to minimize AI-associated arthralgia are scarce. Limited experience suggests that regular exercise, and possibly vitamin D supplementation, may help alleviate symptoms. An update on the syndrome will be presented.

### Cachexia and the Role of Cytokines

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Cachexia is characterized by weight loss, poor appetite, muscle wasting, and decreased survival. Cachexia is generated by tumor-host interactions that produce an aberrant pro-inflammatory response and neurohormonal dysfunction. Evidence suggests that cytokines are important in decreasing the production and increasing degradation of myosin. As a single factor, tumor nuclear-factor (TNF)- $\alpha$  does not consistently produce cachexia; however, in combination with other cytokines (eg, interferon), these factors trigger a selective reduction in the expression of the myosin heavy chain. Animal models of cancer cachexia also show that interleukin (IL)-6 selectively degrades myosin as a result of increased activation of the ubiquitin

ligase-dependent proteasome pathway. Unfortunately, there is no consistent clinical correlation between cachexia and the serum concentration of cytokines. Initial studies in pancreatic and lung cancer patients revealed that higher levels of IL-6 were associated with poor performance status and weight loss. More recently, however, a multi-institutional trial concluded that serum cytokines provide data of limited clinical value in cachexia, since no correlations were observed between serum cytokine concentrations and changes in weight or appetite. A likely explanation for this finding is that local production and action of cytokines within muscle may be more important than systemic levels. Finally, intervention studies targeted at specific pro-inflammatory cytokines have also produced variable benefits. Although small trials of monoclonal antibodies to IL-6 appear promising, a large trial of a TNF inhibitor showed no benefit when compared with placebo. In the future, single nucleotide polymorphisms (SNPs) coding for pro- and anti-inflammatory cytokines may have a role in identifying those patients predisposed to cachexia.

## Pathogenesis and Treatment of Dyspnea

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Dyspnea is a common symptom in patients with lung cancer. Shortness of breath can severely impair patients' quality of life by limiting their physical and social functioning. The pathogenesis of dyspnea in a patient with lung cancer is complex, with multiple factors impacting the perception of its intensity. The pathophysiologic mechanisms of dyspnea can be categorized as impaired ventilation with a restrictive or obstructive ventilatory deficit (or both); increased ventilatory demand; or a combination of these two mechanisms. The causes of dyspnea fall into four categories: direct tumor effects, indirect tumor effects, treatment-related effects, and problems unrelated to the cancer. Optimal treatment of dyspnea requires a thorough assessment of the causes and, potentially, both pharmacologic and nonpharmacologic interventions. This presentation will review the evidence for the use of opioids, anxiolytics, phenothiazines, and other interventions.

## Integrating Supportive and Palliative Care into Oncology

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During the past several decades, there have been dramatic strides in the treatment of patients with cancer. Nitrogen

mustard was the first chemotherapy drug ever used, a history that dates back over 50 years. The development of combination chemotherapy saw improved response rates and prolongation of survival. In the new century, there has been much interest in molecular targeted agents. The most dramatic successful examples have been trastuzumab (Herceptin) in breast cancer and imatinib (Gleevec) in chronic myelogenous leukemia and gastrointestinal stromal tumor. Other new agents include erlotinib (Tarceva), cetuximab (Erbix), sorafenib (Nexavar), and sunitinib (Sutent). Despite these advances, quality of life for patients with cancer still remains a major unmet need. Although significant improvements have taken place in the management of cancer-related pain and chemotherapy-induced nausea and vomiting, further advances are clearly needed. Cancer-related fatigue remains a black hole in oncology, due to its multifactorial cause and complicated treatment. Late complications in curable neoplasms such as testicular cancer deserve special attention. Appropriate follow-up for such patients, with regard to cancer recurrence, preventative medicine, and problem awareness is essential for the maintenance of good health in this young patient population.

## Skeletal Complications: Bisphosphonate- vs Radiation-Induced Osteonecrosis of the Jaw

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Bisphosphonate compounds are powerful inhibitors of osteoclastic activity. Given their long half lives, they can bind to bone for years, making them highly effective in reducing adverse skeletal events in patients with osteoporosis and Paget's disease of bone. Bisphosphonates' antiangiogenic and antineoplastic properties have also led to their use as chemotherapeutic adjuncts for some metastatic carcinomas and malignancies such as multiple myeloma. Despite their therapeutic and prophylactic efficacy, intravenously delivered, nitrogen-containing bisphosphonate compounds appear to have an association with osteonecrosis of the jaw (B-ONJ), a distinctly uncommon but significant complication of therapy that shares some features with osteoradionecrosis (ORN). Although B-ONJ and ORN are histopathologically indistinguishable from one another, their respective clinical presentations and management may differ. It is hypothesized that, given the unique physiologic stresses on the jawbones that demand constant repair of function-generated micro-defects, jawbones rendered relatively hypovascular and hypodynamic from bisphosphonate treatment may have impaired capacity for self repair, resulting in osteonecrosis. However, with a lack of substantive scientific research to date, it is unclear as to whether a bisphosphonate acts alone or in concert with other factors to produce ONJ, since many patients taking bisphosphonates typically have a host of comorbidities that could contribute to this challenging oral-maxillofacial

complication. It is also possible that genetic polymorphisms in an as-yet unidentified subset of individuals create susceptibility to B-ONJ. This presentation will discuss possible risk factors and the diagnostic criteria for B-ONJ and ORN while emphasizing that the benefits of bisphosphonate therapy and radiation therapy far outweigh the risk of developing jaw necrosis.

### **Grief and the Course of Illness**

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Cancer patients and their families face numerous losses during the trajectory of their cancer experience, ranging from the loss of their expected time horizon for the future to the loss of income and role functions. There are also events, aside from cancer, that can sometimes produce overlapping dimensions of loss. Loss results in grief responses, and there are a variety of coping styles—some helpful and some more destructive—that are commonly employed by patients and families. Learning to rewrite one's life narrative in a healthy way is part of creative adaptation. This presentation will describe methods for screening and assessment, as well as the management of uncomplicated and complicated grief by using case vignettes to explore loss and grief in the course of illness.

### **Cognitive Impairment Associated with Breast Cancer Therapy**

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Anecdotal reports of “chemobrain,” or the loss of mental acuity associated with chemotherapy administration, are well publicized among women with breast cancer and are a source of significant concern. Although self-reported cognitive complaints are generally not related to objective neuropsychologic evidence of cognitive impairment in cancer patients, a growing body of research suggests that these concerns are merited. This presentation will summarize the results of studies that have evaluated cognitive functioning in women who are currently undergoing or were previously treated with adjuvant chemotherapy for breast cancer. Particular attention will be devoted to studies that feature such methodologic strengths as a pretreatment baseline assessment, one or more follow-up assessments, the use of a comprehensive battery of neuropsychologic measures, and the inclusion of no chemotherapy or no cancer comparison groups. In addition to summarizing the positive and negative evidence

for chemotherapy-related cognitive problems, the presentation will review mechanisms by which chemotherapy could result in negative changes in cognitive functioning. These mechanisms include the effects of other symptoms (eg, depression and fatigue) as well as the effects of estrogen reduction, genetic susceptibility, and cytokine deregulation on cognitive functioning. The presentation will conclude with a discussion of possible intervention strategies (both pharmacologic and nonpharmacologic) for addressing treatment-related cognitive problems in this patient population.

### **Chronic Graft-Versus-Host Disease: Supportive Care**

*Stephanie J. Lee, MD, MPH*

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Chronic graft-versus-host-disease (GVHD) is a major cause of morbidity and mortality following allogeneic hematopoietic cell transplantation (HCT). People with chronic GVHD report lower physical and functional status and more bothersome symptoms than people who have been treated similarly but do not have chronic GVHD. Although systemic immunosuppressive therapy is the mainstay of chronic GVHD treatment, a wide variety of supportive care measures can improve symptoms and quality of life. This session will review the current state of knowledge about the role of supportive care in optimizing health for people with chronic GVHD and describe the major types of supportive care. We will review data about the effectiveness, accessibility, and cost of supportive care interventions. Finally, we will discuss important areas for future research.

### **Functional Outcomes in Patients With Head and Neck Cancer**

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Head and neck cancer frequently results in functional sequelae, including changes in or the loss of human voice, disruptions in speech production, and swallowing deterioration. These problems may occur because of the disease or its treatment, surgery, radiation therapy, or chemotherapy, alone or in combination. Adjuvant treatments, including radiation therapy, generally increase functional deficits. Chemotherapy that intensifies the effects of radiation therapy may exacerbate functional deterioration, but this relationship remains unproven. Recent data suggest that induction chemotherapy does not produce the functional deterioration commonly reported after definitive treatment regimens for head and neck cancer. In fact, patients'

perceptions of their swallowing ability and diet levels improve despite a lack of change in swallowing physiology. Exercise regimens based on the results of instrumental testing that are designed to strengthen and maintain range of motion, muscle elasticity, and mobility are the best prevention of long-term swallowing dysfunction following head and neck irradiation. When organ preservation protocols fail to successfully safeguard both anatomy and physiology, chronic aspiration and the inability to eat by mouth may relegate the patient to a tracheostomy tube and a gastrostomy tube. Current advances in rehabilitation and restorative technology show that complete surgical resection may produce better functional outcomes and superior quality of life than treatment that spares but cripples the organ; such is the case for patients with laryngeal cancer. Prospective multidisciplinary collaboration is critical to ensure the best oncologic and functional outcomes for optimal quality of life for patients with head and neck malignancies.

## Diagnosis and Management of Malignant Spinal Cord Compression

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Malignant spinal cord compression (MSCC) is a devastating complication of advanced malignancy. Approximately 2.5% of patients dying of cancer will have at least one episode of MSCC, 98% of which will be due to extradural compression. Magnetic resonance imaging is the gold standard for the diagnosis of MSCC. Studies in Britain, Canada, and Israel show that significant intervals are observed between the onset of symptoms and treatment and that functional deficit worsens during these intervals. Options for treatment include surgery, irradiation, or combinations of the two. Good palliative care is essential after the diagnosis. The presentation will also address future directions for research.

## Opioids and Adjuvant Analgesics for Neuropathic Cancer Pain

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Neuropathic pain syndromes can be devastating to individuals with cancer, particularly those with disease that can be treated to obtain long survival or, in some cases, that may be potentially cured. Examples of neuropathic pain syndromes seen in the oncology setting include post-thoracotomy syndrome, chemotherapy-induced peripheral neuropathy, and radiculopathy from metastases to vertebral bodies. Many other pain syndromes

can be associated with nerve damage, leading to sensations such as burning, tingling, electrical, shooting, and painful numbness. These neuropathic pain syndromes are often difficult to manage, yet treatment is available. Opioid therapy, despite past beliefs regarding its ineffectiveness in the management of neuropathic pain, has been found to be useful. Adjuvant analgesics, including corticosteroids, antiepilepsy drugs, antidepressants, local anesthetic agents, and others also have been demonstrated to provide relief. This presentation will review current data regarding the efficacy of these therapies, as well as recommendations regarding their use. Additionally, new drugs in development for the treatment of neuropathic pain will be described.

## Current Models on the Biology of Depression in Cancer

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Depression is a frequent—and profoundly painful—burden borne by many patients with cancer. In addition to the manifold stressors that accompany serious illness, increasing data suggest that activation of the inflammatory arm of the immune system as a result of cancer and/or its treatment may also play an important role in promoting depression in oncology patients. Moreover, it is now recognized that psychologic stress itself activates the same inflammatory pathways triggered by illness. To evaluate mechanisms by which inflammatory activation induces depression, our group has been studying patients receiving the innate immune cytokine interferon (IFN)- $\alpha$  for malignant melanoma and hepatitis C virus (HCV) infection. Chronic treatment with IFN- $\alpha$  is associated with a high rate of depression. Depression in the context of IFN- $\alpha$  is symptomatically similar to idiopathic major depression and responds to treatment with antidepressant medication, further strengthening the argument that cytokine activation is sufficient to induce depression. This talk will explore what IFN- $\alpha$  has taught caregivers about how inflammation changes the central nervous system (CNS) and outflow pathways from the CNS in ways that promote depression; the discussion will also review the value of behavioral interventions such as meditation, which reduce the inflammatory responses to psychosocial stress.

## Communicating With Patients With Cancer

*Lidia Schapira, MD*

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This presentation will begin with a film featuring four patients living with advanced cancer. Through their voices

and experiences, we will learn about their common worries and deepen our understanding of their coping strategies and styles. The film is divided into sections that highlight common concerns and frequent themes and will help frame the didactic comments and interactive discussion. Topics that will be covered include relationships between cancer patients and healthcare professionals, spirituality, hope, managing expectations, and coping. We will invite comments from participants and conclude with a summary of lessons learned and practical tips for clinical practice. The film is *Voices from the Lived World of Illness: Advanced Cancer*, produced by the Center for Communication in Medicine (Bennington, VT).

### **Biology and Management of Constipation in Cancer Patients**

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Normal gastrointestinal function involves the complex integration of neurocrine, endocrine, and autocrine systems. Cancer, its therapy, and pre-existing conditions all have the potential to disrupt this communication, which may result in constipation. An understanding of this pathophysiology can guide how we treat cancer-related constipation as well as target areas for new research. Unfortunately, there is a dearth of evidence on which to base treatment strategies, but an understanding of the therapeutic mechanisms of available laxatives can lead to a rational, empirically-based treatment strategy.

### **Biology and Management of Mucositis Due to Chemotherapy**

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The learning objective of this talk is to become knowledgeable in the epidemiology, pathobiology, clinical presentation, and management of chemotherapy-induced oral mucositis in cancer patients. Oral mucositis is a frequent cause of chemotherapy dose delays and interruptions of cancer therapies. The hallmark feature of mucositis is mouth pain, which can impact a patient's ability to eat, speak, and swallow, resulting in significant morbidity and increased resource utilization. Research into both prevention and management has lagged behind that of other common cancer treatment-related morbidities, such as nausea/vomiting and cytopenias. Although there has been a relative paucity of clinical trials focusing on mucositis as an outcome, recent advances in our understanding of its pathobiology have led to the development of a number of targeted interventions, some of which are currently under clinical investigation. Expert guidelines for the management of mucositis based on critical review of the literature have been recently published; large-scale integration of these guidelines into clinical practice will help improve the overall quality of cancer care provided. Unfortunately, management in large part continues to rely on supportive care and symptom palliation. Regardless, frequent assessments and early and aggressive intervention can reduce the risk of dose reductions or breaks in therapy, which can adversely affect treatment outcomes.