Cancer Neuropathic Pain: Overview of Current Status and Future Objectives

FREDERICK H. HAUSHEER,a–d KATHLEEN M. FOLEYe

aBioNumerik Pharmaceuticals, Inc., San Antonio, Texas, USA; bThe Johns Hopkins Oncology Center, Baltimore, Maryland, USA; cThe University of Missouri-Columbia, Columbia, Missouri, USA; dThe University of Texas Health Sciences Center, San Antonio, Texas, USA; eMemorial-Sloan Kettering Cancer Center, New York, New York, USA


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This issue of The Oncologist is focused on issues and challenges in the pathophysiology, diagnosis, management, and advancing innovative treatment of neuropathic pain in cancer patients. A recent expert forum, organized by the National Cancer Institute, covered key areas of future research and treatment for patients with neuropathic pain. This issue of The Oncologist on neuropathic pain in cancer patients is devoted to a brief current description of the state of affairs in this field and the future directions to be taken.

The mechanisms underlying the pathogenesis and pathophysiology of neuropathic pain have not been fully elucidated, and the article by Dr. Gary Bennett [1], a pioneer in the basic neurophysiology and neuropharmacology of cancer neuropathic pain, presents important findings regarding the role of inflammation and neuropathic pain, and describes some exciting new insights into novel potential mechanisms involving toxic effects on mitochondrial physiology that appear to underlie chemotherapy-induced neuropathy. The opportunity for translational applications of this research is an important consideration.

Drs. Cassileth and Keefe [2] describe important approaches that can be helpful in the care of patients with neuropathic pain that are achieved by integrative oncology, which combines mainstream cancer care and evidence-based complementary therapies. The relationship between mind and body to neuropathic pain is an important area that needs more study to identify approaches that are useful interventions for cancer patients with neuropathic pain.

Drs. Backonja and Woolf [3] describe innovative genome-based approaches to elucidating the underlying pathophysiological processes involved in the genesis of cancer neuropathic pain as well as identifying new targets for drug discovery in cancer neuropathic pain. The potential implications of these approaches are substantial for new drug discovery and development that is based on a logical genomic-based characterization of the gamut of human biological systems that may be involved.

Dr. Lema and colleagues [4] discuss the challenges of addressing neuropathic pain in cancer patients as a common coexisting condition, and point out that because appropriate epidemiological research is severely lacking, a full assessment of the magnitude or the extent of this problem in the...
context of the incidence, prevalence, severity, and relative effectiveness of medical interventions is not possible.

High-quality epidemiological research in this field is one of the most important future areas that will help advance new treatments. A key unmet need in the medical knowledge of the scope of this patient population is the need for evaluating multicenter patient populations, and to apply uniform validated diagnostic criteria to characterize the incidence, prevalence, and severity of neuropathic pain in cancer patients; and further, to appropriately classify the etiological and pathophysiological aspects, such as neuropathic pain associated with tumor infiltration, radiation, surgery, chemotherapy, and other etiologies, including paraneoplastic neuropathies.

Dr. Cleeland and colleagues [5] discuss the challenges in assessing and measuring neuropathic pain, and describe new potentially useful approaches that may guide the future formulation and implementation of diagnostic and severity grading assessments that are patient based. They emphasize the importance of validating such approaches so that their diagnostic reliability, sensitivity, specificity, and predictive value can be used objectively for clinical decision making, and can serve as primary endpoint assessments in randomized interventional trials of cancer neuropathic pain. In terms of developing treatment guidelines, there is a pressing need for larger scale, randomized, controlled, multicenter trials comparing treatment interventions. To perform such trials, the ability to reliably assess the prevention and mitigation of neuropathic pain is dependent upon the use of validated instruments—in particular, patient-based questionnaires that can measure the presence, severity, and graded increases or decreases in neuropathic pain in patients.

These meeting presentations highlight the importance of the problem, the limited treatment options, and the lack of understanding of the multiple pain mechanisms, and clearly argue for a comprehensive research agenda that starts with detailed epidemiologic studies using validated instruments and leads to innovative approaches for prevention and treatment.

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Data analysis and interpretation: Frederick H. Hausheer

Manuscript writing: Frederick H. Hausheer, Kathleen M. Foley

Final approval of manuscript: Frederick H. Hausheer, Kathleen M. Foley

**REFERENCES**

1 Bennett, GJ. Pathophysiology and animal models of cancer-related painful peripheral neuropathy. *The Oncologist* 2010;15(suppl 2):9–12.


