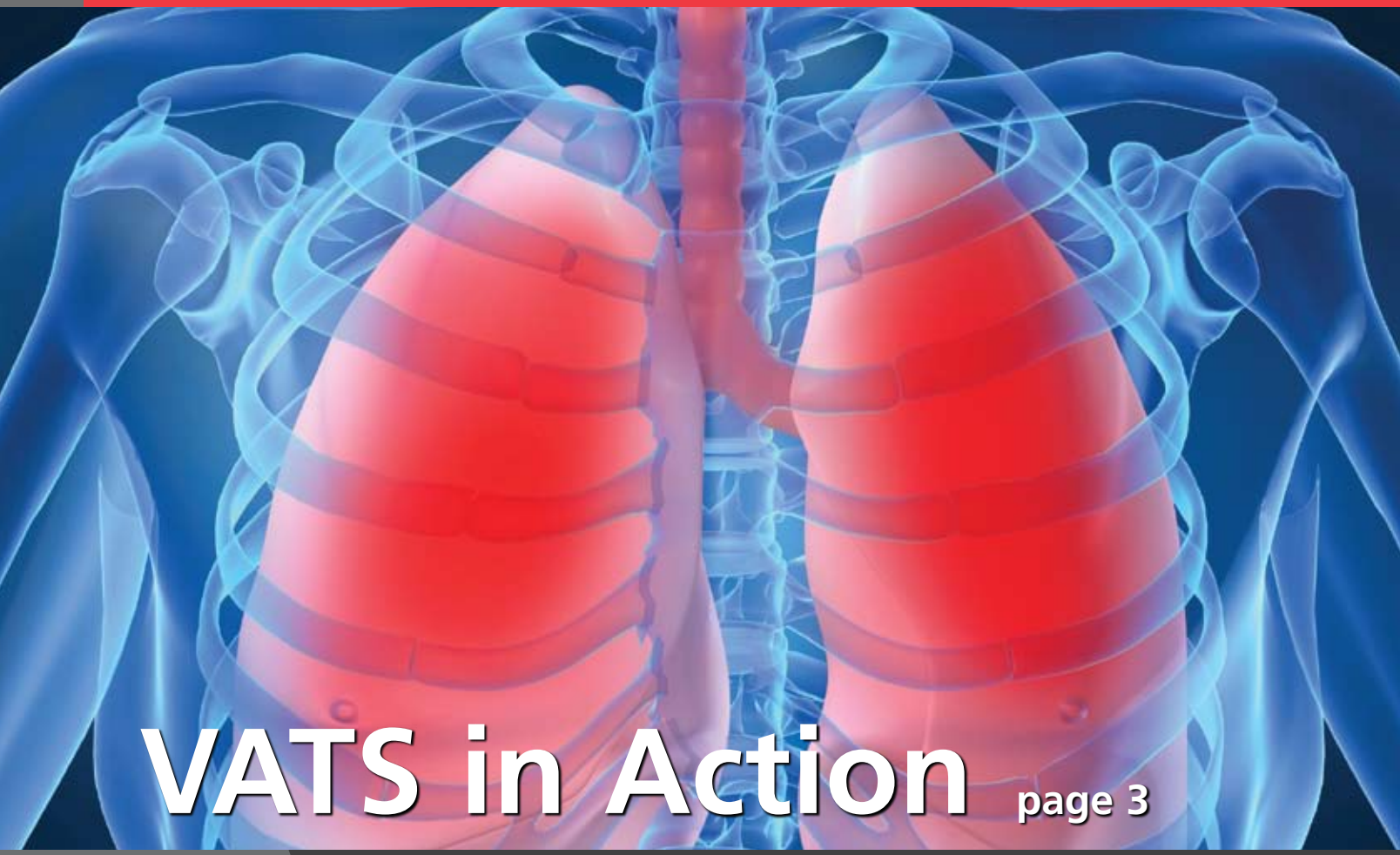
University Hospitals
Case Medical Center

Cleveland | Ohio

UH Innovations In Cancer

University Hospitals Ireland Cancer Center



VATS in Action page 3

A Partner in Care

Welcome to *Innovations in Cancer*, providing examples of our efforts to integrate novel technology and treatments for patients at the Ireland Cancer Center, University Hospitals Case Medical Center.

We are experiencing rapid change and growth. We are recruiting cancer surgeons with expertise in minimally invasive techniques, and expanding the number of novel therapeutics available to our patients through the NCI-supported early phase clinical trials program. Along with our focus on technology, our commitment continues to provide patient- and family-focused care and to ensure continuity of care through excellence in communication with our referring physicians.

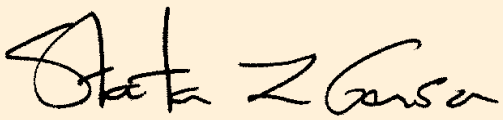
In this edition of *Innovations in Cancer*, we will introduce you to our cancer care teams and highlight a few examples of novel therapeutics. These include video-assisted surgery for lung cancer, directed by **Philip Linden, MD**, and laparoscopic surgery for colorectal surgery, directed by **Conor Delaney, MD, MCh, PhD**, as well as innovative clinical trials led by **Afshin Dowlati, MD**, and **Joseph Baar, MD, PhD**.

At UH Ireland Cancer Center, we provide coordinated cancer care through our disease specific teams that evaluate every patient, collaborating with you to treat your patients. As a tertiary referral center, we can help you review routine and complex case management, including multimodality care and neoadjuvant treatments. With a call to the UH Ireland Cancer Center referral line, an expert can see your patient within 48 hours or you can receive advice anytime. You stay involved in all treatment decisions, and patients quickly return to your care in their hometown.

Given this patient-centered commitment, we are all the more proud that the center once again has been recognized by *U.S. News & World Report* for excellence in cancer care.

I hope you enjoy this issue of *Innovations in Cancer*.

Warm regards,



Stanton L. Gerson, MD
Director, University Hospitals Ireland Cancer Center and
Case Comprehensive Cancer Center

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Contributors: Stanton L. Gerson, MD; Nathan Levitan, MD; Joseph Baar, MD, PhD; Conor Delaney, MD, MCh, PhD; Afshin Dowlati, MD; Philip Linden, MD

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

The commitment to exceptional patient care begins with revolutionary discovery. Faculty at the Case Western Reserve University School of Medicine, who also are physicians at UH Case Medical Center, are at the forefront of medical research and innovation. The School of Medicine is the largest medical research institution in Ohio and among the nation's top medical schools for research funding from the National Institutes of Health.

Video-Assisted Thoracoscopic Surgery

Expanding the indications for minimally invasive cancer surgery while improving outcomes

BY PHILIP LINDEN, MD

Philip Linden, MD, Division Chief, Thoracic and Esophageal Surgery, Ireland Cancer Center at University Hospitals Case Medical Center

Philip Linden, MD, performs a video-assisted thoracoscopic surgery (VATS), a minimally invasive procedure.

Thoracoscopy originated a century ago, when the Swedish internist Hans Christian Jacobaeus reported the first diagnosis and treatment of pleural effusions by thoracoscope. The development of fibro-optic light transmission, additional image processing techniques and related surgical instrumentation enabled the invention of video-assisted thoracoscopic surgery (VATS) in the early 1990s.

Thoracoscopy is still useful in the diagnosis and treatment of pleural effusions. In patients with exudative effusions, thoracoscopy allows for the diagnosis and treatment at the same setting. In patients with a malignant pleural process, if the lung is seen to fully expand under positive pressure ventilation, then talc pleurodesis offers a highly successful treatment. If the lung is unable to expand under positive pressure (either from intrinsic disease, bronchial obstruction or encasement with tumor) then insertion of a drainage catheter allows for palliative drainage at home.

Surgeons with specialized training in VATS continue to expand its applications beyond the treatment of pleural effusions, and the current literature cites several advantages of VATS in both short-term and longer-term surgical oncology outcomes.

REDUCTION IN COMPLICATIONS AND LENGTH OF STAY

A recent propensity-matched analysis of the largest national thoracic surgery database (Society for Thoracic Surgery) has shown fewer complications and shorter length of stay with VATS lobectomy as compared with open lobectomy. VATS patients were more likely than thoracotomy patients to have no complications. VATS lobectomy was associated with a lower likelihood of arrhythmia, reintubation and blood transfusion. The average length of stay for a VATS lobectomy was 4.0 days as compared with 6.0 days for a lobectomy done with a full thoracotomy.

With an experienced team, it is possible to combine a thorough lymph node dissection by a VATS procedure at the time of VATS lobectomy. The thorascopic approach to lobectomy is associated with less blood loss and postoperative pain with little or no change in operative time and a quicker return to baseline function.

NOVEL APPLICATIONS OF VATS

Approximately 75 percent of lobectomies at UH Ireland Cancer Center are done with a VATS approach instead of a large thoracotomy incision; even difficult cases can be done with minimally invasive incisions.

Our surgeons perform VATS segmental resection, a more complex procedure than a lobectomy that preserves more healthy lung tissue and is most useful in patients with impaired lung function, such as emphysema.

UH Ireland Cancer Center surgeons are pioneers in the VATS hybrid approach in patients with cancers metastatic to the lung. This procedure combines a conservative wedge resection for peripheral lesions with ablation of deeper lesions that would otherwise require the removal of an entire lobe of lung. This approach provides the optimal treatment of patients with marginal lung function, and allows for the conservation of lung tissue in patients who are at high risk of developing additional lung metastases in the future.

Ireland Cancer Center at University Hospitals Case Medical Center offers additional options in the treatment of patients with lung cancer who are at high risk of complications from lung surgery, including those with poor lung function or elderly patients. These options range from minimally invasive resection to ablation with CyberKnife® radiation or other ablative techniques. Our expertise in the management of compromised patients along with our multidisciplinary approach gives the patients the best chance of a tailored therapy that is best for them and their quality of life.

Novel Therapeutics

Afshin Dowlati, MD, Director, Thoracic Oncology, Co-Leader, Developmental Therapeutics Program, and the Rosalie and Morton A. Cohen Chair in Lung Cancer at UH Ireland Cancer Center; and Associate Professor of Medicine at Case Western Reserve University School of Medicine

As part of its mission to provide innovative care for patients with cancer, Ireland Cancer Center at University Hospitals Case Medical Center is active in the development and clinical evaluation of a number of novel anticancer agents.

BLP25 LIPOSOME VACCINE IN NSCLC
Principal Investigator: Afshin Dowlati, MD

UH Ireland Cancer Center is participating in the multicenter, international phase III clinical trial of a potential new treatment for non-small cell lung cancer (NSCLC). The Stimulating Targeted Antigenic Responses To NSCLC (START) trial will assess the efficacy and safety of BLP25 Liposome Vaccine (L-BLP25), an investigational therapeutic lung cancer vaccine in patients with unresectable, stage III non-small cell lung cancer who are stable for completing initial therapy. These patients have no other approved medical therapies.

The L-BLP25 vaccine (Stimuvax®) is a liposome-encapsulated peptide vaccine that contains a synthetic peptide derived from the mucin-1 (MUC-1) protein, a high-molecular-weight transmembrane glycoprotein that is overexpressed on the surfaces of many epithelial tumor cells and some B-cell lymphoma cells and multiple myeloma cells. Based on experience in earlier trials, the vaccine is expected to stimulate a cytotoxic T lymphocyte response against tumor cells expressing MUC-1; it is hoped that this cytotoxic response will inhibit NSCLC tumor growth.

> It is hoped that this cytotoxic response will inhibit NSCLC tumor growth.

The trial at UH Ireland Cancer Center is led by **Afshin Dowlati, MD**, Director of Thoracic Oncology, Co-Leader, Developmental Therapeutics Program, and the Rosalie and Morton A. Cohen Chair in Lung Cancer at UH Ireland Cancer Center; and Associate Professor of Medicine at Case Western Reserve University School of Medicine, as part of approximately 250 medical facilities in 30 countries participating in the START trial. The planned enrollment is 1,300 patients with inoperable stage III NSCLC who have completed first-line treatment.

In this placebo-controlled randomized trial, the primary outcome measure is survival. Secondary outcome measures include time to symptom progression, time to disease progression (TTP), one-, two- and three-year survival, and safety. Data collection is expected to be completed at the end of 2010.

Joseph Baar, MD, PhD, FRCP(C), FACP, Medical Oncologist, University Hospitals Case Medical Center; and Associate Professor of Medicine, Case Western Reserve University School of Medicine

IMMUNE RESPONSE TO ANTI-MUC-1 VACCINE IN "TRIPLE NEGATIVE" BREAST CANCER
Principal Investigator: Joseph Baar, MD, PhD, FRCP(C), FACP

Patients with early stage "triple negative" breast cancer (that is, negative for the estrogen, progesterone and human epidermal growth factor 2 (HER2/neu) receptors) are required to have a high risk of recurrences and metastasis. They typically receive initial therapy combining surgery, chemotherapy and radiation therapy. Because these tumors do not express any hormone receptor, further treatment with hormonal therapy or trastuzumab (Herceptin) is not recommended.

Recognizing the need for new therapeutic options, researchers at UH Ireland Cancer Center have determined that the mucin 1 (MUC-1) antigen is expressed in more than 90 percent of triple negative breast cancers, and a vaccine directed against intact MUC-1 has been developed. The vaccine is distinct from that used for NSCLC. The breast cancer vaccine also contains the adjuvant poly-ICLC, which is intended to further boost an immune response against MUC-1. **Joseph Baar, MD, PhD, FRCP(C), FACP**, Medical Oncologist, University Hospitals Case Medical Center; and Associate Professor of Medicine, Case Western Reserve University School of Medicine, is Principal Investigator for a pilot study of this vaccine supported by Avon-NCI in women who have completed therapy for stage I-III triple-negative breast cancer. The objective is to determine whether these patients will develop an adequate immune response to the vaccine as a predictor of improved antitumor immune surveillance. This pilot study is not designed to determine vaccine efficacy in reducing metastases, although future studies of its efficacy may be undertaken if the pilot study determines that a sufficient immune response occurs.

Seventeen patients will be enrolled in the first stage of this study, with an additional 20 patients to be enrolled in a second stage if the first stage results show that the vaccine induces immune responses. The primary endpoint is the proportion of patients showing an immunologic response at week 16 following four injections. Secondary measures include safety and toxicity using National Cancer Institute (NCI) Common Toxicity Criteria (CTC). Results are anticipated after the final data collection occurs in late 2012.

Andrew Sloan, MD, Director, Brain Tumor and Neuro-Oncology Center, University Hospitals Case Medical Center; Associate Professor Peter D. Cristal Chair in Neurosurgery, Case Western Reserve University School of Medicine

Lisa R. Rogers, DO, Neurologist, University Hospitals Case Medical Center; Professor of Neurology, Case Western Reserve University School of Medicine

TRC102

Principal Investigators: Afshin Dowlati, MD; Andrew Sloan, MD; Lisa R. Rogers, DO; Panos Savvides MD, PhD, MPH

The ability of cancer cells to recognize and repair damage to DNA induced by alkylating agents is an important mechanism for therapeutic resistance. TRC102, also known as methoxyamine, is a novel anticancer agent that targets one of the key DNA repair pathways, the base excision repair (BER) pathway. Originally developed within the laboratories of UH Ireland Cancer Center and Case Western Reserve University School of Medicine, TRC102 is now being evaluated in combination with chemotherapy in clinical trials under way at UH Ireland Cancer Center.

Earlier studies demonstrated the ability of TRC102 to enhance the cytotoxic effect of temozolomide and Alimta in human tumor xenograft models. A phase I trial is under way to determine the maximum tolerated dose of TRC102 given in combination with temozolomide in patients with advanced solid tumors. The planned enrollment is 36 patients and includes patients with primary or metastatic CNS disease. Primary outcome measures are the maximum tolerated dose of TRC102 in combination with temozolomide. Since the mechanism is precisely known, the effect of TRC102 on blockade of DNA repair will also be measured. Each continuous infusion study has been simplified to a single one-hour IV administration. DNA strand breaks in blood mononuclear cells are being assessed by comet assay.

Panos Savvides MD, PhD, MPH, Medical Oncologist, University Hospitals Case Medical Center; Assistant Professor of Medicine, Case Western Reserve University School of Medicine

An additional phase 1 study nearing completion is an open label, dose-finding study of TRC102 in combination with pemetrexed in patients with advanced or metastatic solid cancer. Thirty patients were enrolled in the study, which was designed to determine the dose of TRC102 to give in combination with pemetrexed. Successful completion of both studies will lead to phase II clinical trials in melanoma, glioma, lung cancer and other solid tumors.

Enroll with Us

Go to **UHhospitals.org/Irelandcancer** to see a video orientation about how to enroll patients in a clinical trial at UH Ireland Cancer Center.

New Arrivals

Three renowned physicians bring leading expertise to UH Ireland Cancer Center

NEAL J. MEROPOL, MD

Neal J. Meropol, MD, is Section Chief of Medical Oncology, University Hospitals Case Medical Center, and Associate Director for Clinical Programs, UH Ireland Cancer Center. He is also Associate Director of Clinical Research for the Case Comprehensive Cancer Center. Dr. Meropol holds the Dr. Lester E. Coleman, Jr. Chair in Cancer Research and Therapeutics. In addition to his work in developing clinical trials for patients with gastrointestinal cancer, Dr. Meropol conducts research in patient decision-making and doctor-patient communication, with particular interest in barriers to clinical trial participation. One current project is PREACT (Preparatory Education About Clinical Trials), an NIH supported study that uses the Internet to deliver personalized informational video clips to patients to help them better understand clinical trials. Through another NIH grant, Dr. Meropol is investigating the impact of high expectations for treatment benefit on patients' psychological health in the face of bad news. Prior to coming to the UH Ireland Cancer Center, Dr. Meropol was Adjunct Senior Fellow at the Leonard Davis Institute of Health Economics, part of the Wharton School of the University of Pennsylvania, and Senior Member, Division of Medical Science and Division of Population Science at the Fox Chase Cancer Center in Philadelphia.

MITCHELL MACHTAY, MD

Mitchell Machtay, MD, is the Chair of Radiation Oncology at University Hospitals Case Medical Center and the Vincent Smith Professor of Radiation Oncology at Case Western Reserve University School of Medicine. Dr. Machtay is one of the nation's leading clinical researchers in radiation oncology, particularly in the area of combined modality therapy for lung and head and neck cancers. He has authored more than 90 articles, book chapters, reviews and editorials, in addition to numerous abstracts. Dr. Machtay was one of the first investigators to combine taxane-based chemotherapy with radiotherapy in clinical trials for head and neck cancers, which is now a common standard of care. Since 2000, Dr. Machtay has been the Deputy Chair of the Radiation Therapy Oncology Group, the world's leading multicenter radiation oncology clinical trials organization. Other research interests include protection from dose limiting toxicity of chemoradiation for head and neck, lung and brain tumors and the evaluation of biologic therapy added to chemoradiation for these types of malignancies, and the evaluation of biologic therapy added to chemoradiotherapy for advanced head and neck cancer.

University Hospitals Case Medical Center is completing a free-standing 120-bed cancer hospital scheduled to open spring 2011.

PABLO R. ROS, MD, PHD, MPH

Pablo R. Ros, MD, PhD, MPH, is the Chair of the Department of Radiology of University Hospitals Case Medical Center and Case Western Reserve University School of Medicine and Co-Director, Case Center for Imaging Research, Case Western Reserve University School of Medicine. Dr. Ros has held many distinguished positions previously, including Professor of Radiology and Executive Vice-Chair, Harvard Medical School; Associate Radiologist-in-Chief, Brigham and Women's Hospital; and Chief of Radiology, Dana Farber Cancer Institute. Dr. Ros has published more than 250 articles, book chapters and textbooks. His diverse research interests include many topics related to abdominal oncologic imaging, including liver, pancreatic, mesenteric and gastrointestinal cross-sectional imaging with pathologic correlation; evidence-based radiology; and quality management in radiology. Dr. Ros' numerous awards include the Schinz Medal, Swiss Society of Medical Radiology; Gold Medal, Interamerican College of Radiology; Beclere Medal, International Society of Radiology; Academic Excellence Award, Mexican Society of Radiology & Imaging; and a Joint Meritorious Unit Citation from the Armed Forces Institute of Pathology. He holds several editorial positions with leading medical journals. He is also past president of the Society of Gastrointestinal Radiologists.

Pioneering Work in Colon Cancer

The option of laparoscopically assisted surgery has been shown safe and cost effective

BY CONOR P. DELANEY, MD, MCH, PHD

Conor P. Delaney, MD, MCh, PhD, FRCSI, FACS, FASCRS, Chief, Division of Colorectal Surgery; Vice-Chair, Department of Surgery; Director, Institute for Surgery and Innovation; University Hospitals Case Medical Center and Case Western Reserve University

Conor Delaney, MD, MCh, PhD, performs a minimally invasive procedure for colorectal cancer.

Laparoscopic assisted surgery was first considered for use in patients undergoing colectomy for colon cancer in 1990. Several concerns were raised, however, including questions of how well laparoscopic surgery would compare with conventional open colectomy in achieving proper resection, whether it would provide adequate information about staging, and whether it would result in higher rates of tumor recurrence at wound and trocar sites. A literature review published in 2001 attempted to answer some of these critical questions, but the author found that little high-level data had been published comparing the safety and efficacy of laparoscopic-assisted resection of colorectal malignancies with open colectomy. The data that were available seemed to indicate no difference in perioperative mortality, long-term survival, complications, lymph node harvest or resection margins. The available literature also included reports of increased operative time (by about 50 minutes) and decreased hospital stay (reduced from eight to six days) and time to bowel function.

The first truly comprehensive set of data was provided by a prospective, randomized trial that compared laparoscopically assisted and open surgery for curable colon cancer in 872 patients treated at 48 institutions. The median patient follow-up was 4.4 years, and the primary endpoint for the trial was the time to tumor recurrence. The study began in 1994; results were published in 2004 and provide several important comparisons of the two procedures. The rates of cancer recurrence were similar in the two groups (16 percent for laparoscopically assisted surgery versus 18 percent for open colectomy), with recurrence rates in surgical wounds less than 1 percent in both groups. Overall survival was also similar (86 percent laparoscopic versus 85 percent open) with no significant difference between groups in the time to recurrence or overall survival for patients with any stage of cancer. Faster recovery and briefer use of parenteral narcotics and oral analgesics were reported in the patients with laparoscopic surgery versus the open colectomy group. The two groups did not differ in rates of intraoperative complications, 30-day postoperative mortality, complications at discharge and 60 days, hospital readmission, and reoperation.

Additional studies also support the conclusion that laparoscopically assisted surgery for colorectal cancer is very reliable when performed by an experienced colorectal surgeon. Physicians at University Hospitals Ireland Cancer Center have extensive experience in minimally invasive colon cancer surgery and consider it an important option for patients. The surgery has been shown repeatedly to be safe and cost effective, with accelerated postoperative recovery and fewer postoperative complications for patients with cancer. Hospital stay is reduced by an average of two days, and time to full recovery reduced by about 50 percent. No differences have been found in tumor recurrence rate or overall cancer survival rate. This minimally invasive surgery is currently considered the optimal approach for most colon cancers, and many rectal cancers, although further studies continue to be performed at UH Ireland Cancer Center and other institutions for the assessment of its use for rectal cancer surgery.

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INNOVATIVE TREATMENT

The Right Note

Music therapy supports oncology patients

BY DEFORIA LANE, PHD, MT-BC

Deforia Lane, PhD, MT-BC, Director, Music Therapy, and Associate Director, University Hospitals Ireland Cancer Center, and Assistant Clinical Professor of Medicine at Case Western Reserve University School of Medicine

Music therapy is an important aspect of treatment for inpatients and outpatients at the Ireland Cancer Center at University Hospitals Case Medical Center. We strategically use it in our community outreach programs.

THE ROLE OF MUSIC THERAPY

Research studies support music therapy to reduce anxiety, depression, stress and pain, and, when used with anti-nausea drugs for patients receiving high-dose chemotherapy, to reduce nausea and vomiting.

At UH Ireland Cancer Center, we individualize our use of music to embrace the culture, ethnicity and the most immediate needs of patients and families. We integrate the latest neurology and music therapy techniques to address patients' physical, psychosocial and spiritual goals. Our aims are to (1) communicate clearly and with compassionate care; (2) acknowledge the patient's challenges and coping skills; and (3) empower both patient and family with evidence-based support offered by music therapy. We use patient-preferred, live music whenever possible.

INPATIENT SETTING

We provide procedural support for inpatients undergoing difficult or fear-invoking procedures such as bone marrow aspirations, biopsies, painful dressing changes and injections. Neurologic music therapy techniques can help oncology patients increase muscle tone, strength and endurance; organize motor planning to improve gait; and increase mobility.

OUTPATIENT SETTING

During chemotherapy we use music-assisted relaxation and imagery and reframing techniques to focus patient attention during needle insertion, transitions, painful episodes and other anxiety-provoking procedures. In addition to monitoring vital signs, we survey patients to determine their view of music's effectiveness. Our average patient response is an 8 on a Likert scale of 1-10.

IN THE COMMUNITY

As an ongoing part of the UH Ireland Cancer Center outreach programs, we provide music therapy twice each month at Hope Lodge to promote positive, meaningful socialization and self-expression for patients and families who reside there during treatment. We also created the unique community program "Sing, Sister, Sing" in which three African American women, patients at UH Ireland Cancer Center, tell their story of cancer in a short skit/drama and sing the songs that encouraged them through the journey. (I am one of them.) We have reached hundreds of inner city women in Cleveland over the past four years and expanded the program to several states. This outreach to the underserved educates, debunks myths and inspires while emphasizing the importance of mammography and breast self-exam.

Deforia Lane, PhD, MT-BC, and music therapy intern Amy Wilson engage patients (and families) in a music therapy session on the unit.

RESEARCH

We are involved in research studies at UH Ireland Cancer Center to evaluate the effects of music therapy in various settings and welcome opportunities to collaborate with physicians and nurses.

Meet the Team

Additional members of the Music Therapy Team at UH Ireland Cancer Center are Maria Hernandez, MD, MT-BC; Kathy Jo Gutgsell, RN, MT-BC, NMT; Diana Le, MT-BC, NMT; and two music therapy interns. Five interns are mentored each year; 60 have been through the 25-year program to date. They come from all over the United States and abroad. They must have a bachelor's or an advanced degree and complete 1,040 hours of hands-on internship before taking the national board exam for MT-BC certification.