

# 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.

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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.



**TRC102**

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



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

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



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



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

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.

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](http://UHhospitals.org/Irelandcancer) to see a video orientation about how to enroll patients in a clinical trial at UH Ireland Cancer Center.