Dear Friends and Colleagues,

It gives me great pleasure to participate in this issue of Lung Cancer Link. Radiation Oncology here at the UWCCC has undergone major changes over the last few months. We have now expanded into the lower level of the Wisconsin Institutes for Medical Research (WIMR). With nearly three times the space, we will be able to continue to build upon our multidisciplinary expertise in lung cancer. Several new technologies have developed within the Radiation Oncology department. We now have the ability to treat early stage non-small cell lung cancer non-invasively in using Helical Tomotherapy with just five treatments with control rates near 90%. This has been a tremendous improvement on the previous standards of 33 treatments with only a 40% control rate.

For patients that are borderline candidates for a lobectomy due to poor pulmonary function, we have recently introduced brachytherapy in the operating room with Dr. Weigel. In these situations, we are able to deliver a high dose of radiation just along the staple line of a wedge resection using radioactive Iodine-125 seeds embedded in a mesh that is placed over the staple line.

For patients with more high-risk disease, we are able to utilize new image-guided technologies, such as Helical Tomotherapy, to ensure we are treating the tumor while sparing normal tissue more effectively. This has allowed us to reduce the side effects of radiation while escalating the dose to the tumor in the hopes of improving our clinical efficacy.

We are very proud of the progress we have made in the lung program over the last several years. The collaborative efforts of not only the participants in the lung program here at UW, but also the physicians and patients of Wisconsin and Northern Illinois have allowed us to get to where we are today. With your continued support, we will be able to continue improve cancer treatment for our patients.

Sincerely,

Deepak Khuntia, MD
Assistant Professor
Director, Radiation Oncology Residency Program
Department of Human Oncology
Our Featured Protocols

A Double-Blind, Randomized, Placebo-Controlled Phase III Study to Assess the Efficacy of recMAGE-A3 + AS15 Antigen-Specific Cancer Immunotherapeutic as Adjuvant Therapy in Patients with Resectable MAGE-A3-Positive Non-Small Cell Lung Cancer

The 5-year disease-free survival (DFS) of patients with stage IB-II NSCLC is 62% for those who receive adjuvant chemotherapy and approximately 50% for those who do not receive chemotherapy. The DFS is considerably less when the whole early stage (IB-IIIA) population is considered. Currently, adjuvant chemotherapy is the standard of care for stage II and IIIA NSCLC, and is also considered for some high-risk stage IB NSCLC patients who have had their cancer completely resected. However, more than 50% of these patients will relapse. Because of the high and rapid rate of recurrence, there is a clear medical need for more effective treatment in this population.

MAGE-A3 is a gene that encodes a tumor-specific antigen, and is silent in all normal human tissues except the testis. Because MAGE-A3 is highly tumor specific, targeting MAGE-A3 with an antigen-specific cancer immunotherapeutic is expected to be well tolerated. The aim of this novel study drug is to immunize patients against the antigens that are expressed by their tumor cells, and thereby eradicate these tumors. The interest in rec-MAGE-A3 immunotherapy is further reinforced by the possible link between MAGE-A3 expression and shorter survival.

Study Design

Administration of up to 4 cycles of adjuvant platinum based chemotherapy is allowed between surgery and randomization to the study. Patients who are likely to meet the eligibility criteria will be asked to allow for MAGE-A3 testing on their tumor tissue. If the patient’s tissue shows adequate expression, the patient will receive rec-MAGE-A3+AS15 or placebo intramuscularly every 3 weeks for 5 cycles, then an additional 8 doses every 3 months thereafter.

A Phase I, Intrapatient Dose-Escalation Study of Sorafenib in Advanced or Relapsed Non-Small Cell Lung Cancer (NSCLC)

Sorafenib (BAY 43-9006) is an oral multi-kinase inhibitor with effects on tumor proliferation and tumor angiogenesis. Sorafenib has inhibitory activity against the serine/threonine kinases Raf-1 and wild-type B-Raf, which are pivotal components of the Ras/Raf/MEK/ERK signaling pathway which induces genes involved in tumorigenesis, angiogenesis, and apoptosis. Inhibitory activity has also been demonstrated against the tyrosine kinases for vascular endothelial growth factor (VEGF 1, 2, and 3) receptor and platelet-derived growth factor (PDGF) receptor as well as Flt-3 and c-Kit.

The safety and clinical activity of sorafenib, alone or in combination with chemotherapy, has been examined in a series of phase I studies conducted in patients with solid tumors with a maximum tolerated dose reached of 400mg BID dosed continuously.

Non-small cell lung cancer is a heterogeneous disease clinically and molecularly. Several targeted agents have been approved for the treatment of advanced non-small cell lung cancer—bevacizumab, erlotinib, gefitinib—though these agents represent only modest improvements and likely fail, in part, because they target a single transduction pathway. Sorafenib, with its multikinase inhibition, is an interesting agent to investigate in advanced lung cancer as it may block salvage pathways or escape mechanisms for cell survival.

Study Design

A phase I, intra-patient dose escalation design of sorafenib, dosed continuously on a 28-day cycle, using 3 primary dose levels: 400 mg orally daily, 400 mg orally twice daily days 1 - 28, 600 mg orally twice daily days 29 – 56, and 800 mg orally twice daily thereafter. Enrollment for all patients will begin at 400 mg daily. Individual patients will be dose escalated (or de-escalated) until they have dose limiting toxicity or reach 800 mg twice daily.

The objectives of the study are to establish efficacy of rec-MAGE-A3 in the chemotherapy and non-chemotherapy arms and to examine gene expression and possible correlation with clinical outcome.

Protocol Eligibility*

- Inclusion Criteria: Histologically confirmed NSCLC stage IB, II, or IIIA that has been surgically removed involving at least a lobectomy, tumor must be positive for MAGE-A3 expression
- Exclusion Criteria: Primary tumor removal by segmentectomy or wedge resection, use of systemic corticosteroids, uncontrolled congestive heart failure or hypertension, use of home oxygenation.

Protocol Eligibility*

- Inclusion Criteria: Advanced (stage IIIB with pleural effusion, stage IV, or recurrent) NSCLC; must have received 2 prior chemotherapy regimens (not including erlotinib or gefitinib)
- Exclusion Criteria: Untreated or unstable brain metastasis, Performance status of 2 or more, uncontrolled hypertension, congestive heart failure

*Select eligibility requirements
# Chemotherapy Protocols

## Non-Small Cell Lung Cancer (NSCLC)
- **Phase I Study of Erlotinib and Sunitinib in NSCLC.**
- **A Combined Phase I and II Study Investigating the Combination of RAD001 and Erlotinib in Patients with Advanced NSCLC Previously Treated Only with Chemotherapy.**
- **A Phase II Study of Cetuximab for the Treatment of Patients with Advanced Bronchioalveolar Carcinoma (BAC) or Adenocarcinoma with BAC Features.**
- **A Phase I Sequential Cohort, Dose Escalation Trial to Determine Safety, Tolerability, and Maximum Tolerated dose of Weekly Administration of GRN163L in Combination with Paclitaxel and Carboplatin in Patients with Advanced or Metastatic NSCLC.**
- **A Phase II/III Randomized, Double-Blind Study of Paclitaxel plus Carboplatin in Combination with Vorinostat (MK-0683) or Placebo in Patients with Stage IIIB (with pleural effusion) or Stage IV NSCLC.**
- **A Phase III Randomized Trial of Adjuvant Chemotherapy with or without Bevacizumab for Patients with Completely Resected Stage IB (≥ 4 cm) – IIIA NSCLC**
- **A Phase III Randomized Trial of Lobectomy Versus Sublobar Resection for Small (< 2 cm) Peripheral NSCLC.**
- **A Randomized Phase III Study of Sublobar Resection Versus Sublobar Resection plus Brachytherapy in High Risk Patients with NSCLC, 3 cm or Smaller.**
- **A Double-Blind, Randomized, Placebo-Controlled Phase III Study to Assess the Efficacy of recMAGE-A3 + AS15 Antigen-Specific Cancer Immunotherapeutic as Adjuvant Therapy in Patients with Resectable MAGE-A3-Positive NSCLC.**
- **A Randomized Phase 2 Study of Maintenance Temozolomide Versus Observation in Stable and Responding Stage IIIB/IV NSCLC Patients.**
- **A Phase I, Intrapatient Dose-Escalation Study of Sorafenib in Advanced or Relapsed NSCLC.**
- **A Phase II Trial of Vorinostat (SAHA, Zolinza®) and Bortezomib (PS341, Velcade®) as Third-Line Treatment in Patients with Advanced NSCLC.**

## Small Cell Lung Cancer (SCLC)
- **An Open-label, Multi-Center, Non-comparative, Phase II study of Oral Topotecan in Combination with Bevacizumab for Second-line Treatment in Subjects with Relapsed SCLC.**

# Radiation Protocols

- **The Use of Helical Tomotherapy to Achieve Dose-per-fraction Escalation in Lung Cancer.**
- **Phase I Study of Image Guided Stereotactic Body Radiotherapy for Small Lung Malignancies.**
- **Phase III Trial Comparing Whole Brain Radiation and Stereotactic Radiosurgery Alone versus with Temozolomide or Gefitinib in Patients with NSCLC and One to Three Brain Metastases.**
- **An Open-label, Multi-Center, Phase II Study to Evaluate the Activity of Patupilone (EPO906), in the Treatment of Recurrent or Progressive Brain Metastases in Patients with NSCLC.**
- **Phase III Randomized Trial of the Role of Whole Brain Radiation Therapy in Addition to Radiosurgery in Patients with One to Three Cerebral Metastases.**
- **Phase I Trial of Helical Tomotherapy Simultaneous Boost (SIB) Treatment for Patients with Brain Metastases.**

# Other Protocols

- **Fluorescence Bronchoscopic Surveillance for New Lung Primaries after Curative Therapy for Squamous Cell Carcinoma of the Aerodigestive Tract.**
- **Randomized Phase III Study of Sublobar Resection versus Sublobar Resection plus Brachytherapy in High Risk Patients with NSCLC, 3 cm or Smaller.**
- **Molecular Epidemiology Case-Series Study of NSCLC in Smoking and Non-Smoking Women and Men.**
- **Molecular Markers for NSCLC Susceptibility.**
- **Preoperative Oncogeriatric Assessment for Thoracic Malignancies (TOGA).**

For more information about referring patients to the UW Paul P. Carbone Comprehensive Cancer Center, call Cancer Connect at (800) 622-8922 or (608) 262-5223.
Lung Cancer is the leading cause of cancer death in the United States.

Lung cancer symptoms include a persistent cough, coughing up blood, changes in breathing, repeated bouts of pneumonia or bronchitis, chest or rib pain, fatigue, lethargy, loss of appetite, and weight loss.

The UW Paul P. Carbone Comprehensive Cancer Center is one of 39 NCI-designated comprehensive cancer centers in the country.

Did You Know?