As Director of the Lung Cancer Program at the University of Wisconsin Carbone Cancer Center, I am pleased to tell you about a transformative step we will be taking this Autumn. Members of our Multidisciplinary Lung Cancer team will be moving into the Wisconsin Institutes for Medical Research (WIMR). This state-of-the-art research building was completed in late 2008 and is adjacent to UW Hospital and Clinics. It is seven floors tall and measures 30,000 square feet per floor.

WIMR will serve as the focal point as our research program transforms into one that centers on translational discoveries, creating new treatments from new science. Our Multidisciplinary Lung Cancer team will share the third floor of WIMR with clinical and laboratory researchers who focus on head and neck cancer. This partnership takes advantage of the biology and treatments shared by both lung cancer and head and neck cancer. Our floor houses eight large laboratory bays that will be filled with scientists and trainees dedicated to investigating the underlying biology of lung cancer. Six laboratory scientists from the UW campus have already committed to joining us in WIMR and adding lung cancer to their research portfolios, leaving two laboratories to be filled by incoming recruits. These six cancer laboratory scientists already have expertise in angiogenesis, lymphangiogenesis, EGFR biology and resistance to EGFR inhibition, and in mechanisms of DNA damage and repair.

Clinical researchers, including myself and my medical oncology colleagues from the UW Multidisciplinary Lung Cancer team, will occupy office space alongside the laboratory scientists on our floor. We believe WIMR provides an ideal setting in which to develop translational research endeavors that can incorporate the latest discoveries in basic oncology research into clinical research projects in a seamless “bench-to-bedside” transition. Members of the UW Multidisciplinary Lung Cancer team believe that it is only through applying the most recent scientific advances in lung cancer biology that improvements will be gained in the prevention, early detection, and in the treatment of this devastating disease.

I invite you to review this newsletter. We look forward to updating you in the future about our translational research projects arising from our WIMR team.

Sincerely,

Anne Traynor, MD
Director
UW Multidisciplinary Lung Cancer Team
Section of Hematology/Medical Oncology

UW Carbone Cancer Center

Anne Traynor, MD
**A Phase I Dose-Escalation Study of the Safety of XL147 in Combination with Carboplatin and Paclitaxel in Patients with Advanced Solid Tumors**

XL147 is an oral selective inhibitor of the phosphatidylinositol 3-kinase (PI3K) pathway, which is frequently dysregulated in cancer cells. In preclinical xenograft tumor models XL147 inhibited tumor growth when given as a single agent, and enhanced the anti-tumor effects of paclitaxel or carboplatin. A single agent Phase I study demonstrated that XL147 is generally well tolerated. The most common side effects were rash and nausea. Inhibition of the PI3K pathway was seen in tumor and skin biopsies from patients with various solid tumors (Shapiro G, et al. Proc ASCO 2009, abstract #3500).

**Study Design**

The primary objective is to evaluate the safety and tolerability of this treatment combination. XL147 is administered orally on a continuous daily dosing schedule. Carboplatin and paclitaxel are administered intravenously on day 1 of each 21-day cycle. Once the maximum tolerated dose of this combination has been identified in patients with advanced solid tumors, an expanded cohort of patients with endometrial cancer, ovarian cancer or non-small cell lung cancer (NSCLC stage IIIB or IV) will be allowed to enroll. The maximum doses of carboplatin in the endometrial and ovarian cancer cohorts will be an AUC of 6 and 175 mg/m² of paclitaxel. For NSCLC the maximum doses of carboplatin will be an AUC of 6 and 225 mg/m² of paclitaxel. Administration of XL147 may continue following completion of carboplatin and paclitaxel.

**A Phase I/II Study of the Safety and Efficacy of TH-302 in Combination with Either Pemetrexed (non-squamous) or Docetaxel (any histology) in Patients with Relapsed Non-Small Cell Lung Cancer (NSCLC) Who Have progressed Through One Prior Chemotherapy**

TH-302 is a hypoxia-targeted prodrug with a 2-nitroimidazole trigger that is activated under hypoxic conditions to release a DNA cross-linker, a bromo analog of the active warhead of ifosfamide. It is minimally toxic to aerobic cells, but is activated to a cytotoxic drug under lower oxygen concentrations than other bioreductive compounds, such as tirapazamine. It has single agent anti-tumor activity in in vivo models of NSCLC and displays additive-to-synergistic tumor growth inhibition when combined with other chemotherapeutics. It has displayed single agent activity in phase I studies in small cell lung cancer and is generally well tolerated, with minimal myelosuppression (Bendell JC, et al., Proc ASCO 2009, abstract #2573). It has also displayed initial combination agent activity as part of the Phase I dose escalation in NSCLC when combined with docetaxel or pemetrexed (Borad M, et al., ECCO 2009, abstract #1266).

**Study Design**

This is a phase I/II dose escalation study of the combination of TH-302 in the second line setting of advanced NSCLC. Patients must have progressed through one prior chemotherapy regimen for their advanced disease. Two arms are open in this study: TH-302 combined with pemetrexed for patients with non-squamous NSCLC, or with docetaxel for patients with any histology of NSCLC. Pemetrexed and docetaxel are given every 21 days, and TH-302 is administered IV on days 1 and 8 of every 21-day cycle.

**Protocol Eligibility**
- ICOG PS 0 – 2
- Fasting blood glucose level ≤ 120 mg/dL
- 4-6 weeks out from prior chemotherapy
- 14 days out from prior erlotinib therapy
- No therapeutic anticoagulation
- No chronic corticosteroid therapy

*Select eligibility requirements*
Our Current Protocols

Chemotherapy Protocols

**Non-Small Cell Lung Cancer (NSCLC)**

- A Phase I, Intrapatient Dose-Escalation Study of Sorafenib in Advanced or Relapsed NSCLC
- A Phase I Study of Erlotinib and Sunitinib in NSCLC
- A Phase II Trial of Vorinostat (SAHA, Zolinfia®) and Bortezomib (PS341, Velcade®) as Third-Line Treatment in Patients with Advanced NSCLC
- A Phase Ib/II Study of AMG 479 in Combination with Paclitaxel and Carboplatin for the First-Line Treatment of Advanced Squamous Non-Small Cell Lung Cancer
- A Randomized Phase II Study of Maintenance Temozolomide Versus Observation in Stable and Responding Stage IIIB/IV Non-Small Cell Lung Cancer Patients
- A Randomized Phase II Study of a Human Anti-PDGFR Monoclonal Antibody (IMC-3G3) with Paclitaxel/Carboplatin or Paclitaxel/Carboplatin Alone in Previously Untreated Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer
- 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
- Phase III Randomized Trial of Adjuvant Chemotherapy With or Without Bevacizumab for Patients With Completely Resected Stage IB (≤ 4cm)-IIIA Non-Small Cell Lung Cancer (ECOG 1505)

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 I Study Evaluation of the Safety, Tolerability and Pharmacokinetics of ABT-888 in Combination with Whole Brain Radiation Therapy in Subjects with Brain Metastases
- Randomized, Phase III, Open Label Study of Oral Topotecan plus Whole-Brain Radiation Therapy (WBRT) Alone in Patients with Brain Metastases from NSCLC
- A Randomized, Phase III, Double-Blind, Placebo-Controlled Trial of Memantine for Prevention of Cognitive Dysfunction in Patients Receiving Whole Brain Radiotherapy

Other Protocols

- Molecular Epidemiology Case-Series Study of Non-Small Cell Lung Cancer in Smoking and Non Smoking Women and Men
- Molecular Markers for Non-Small Cell Lung Cancer Susceptibility
- A Phase III Randomized Trial of Lobectomy versus Sublobar Resection for Small (≤ 2 cm) Peripheral Non-Small Cell Lung Cancer
- Randomized Phase III Study of Sublobar Resection versus Sublobar Resection plus Brachytherapy in High Risk Patients with Non-Small Cell Lung Cancer (NSCLC), 3 cm or Smaller

LINK ➤ A complete listing of all clinical trials at the UW Carbone Cancer Center is also available on our website: http://www.cancer.wisc.edu.

For more information about referring patients to the UW Carbone Cancer Center, call Cancer Connect at:
(800) 622-8922 or (608) 262-5223.
Together We Can Save Lives

Save the Date:

November is Lung Cancer Awareness Month

November 11, 2009:

UW Carbone Cancer Center Grand Rounds

Presenter: Avi Spira, MD, MSc

8:00 – 9:00 am

UW Hospital and Clinics, G5/119 – Clinical Science Center.


November 12, 2009:

Caring for the Lung Cancer Community

Presentations on emerging lung cancer research, complementary medicine, and nutritional and psychological support for lung cancer patients.

Free and open to the public.

6:30 pm: Refreshments and Introduction

7:00 pm: Program

Marriott Hotel,

65119 – Clinical Science Center.

November 11, 2009:

Learn More About UW Multidisciplinary Lung Cancer Team

Did You Know?

The UW Carbone Cancer Center lung cancer specialists take a team approach to treat patients with:

• Small cell lung cancer
• Non-small cell lung cancer
• Mesothelioma
• Bronchioloalveolar carcinoma (BAC)
• Other lung-related malignancies

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