Welcome to the Spring 2012 issue of the Stanford Cancer Institute Clinical Research Newsletter. This quarterly publication is designed to inform our colleagues in the medical community about current clinical trials and research studies available at the NCI-designated Stanford Cancer Institute. In each issue we highlight a number of our more than 300 available clinical trials and novel treatments, including some early-phase clinical trials which are open to patients through our Developmental Therapeutics Program. As the co-leader of the Thoracic Oncology Program and the Principal Investigator of Stanford’s Eastern Cooperative Oncology Group (ECOG) Program, I am delighted to have the opportunity to introduce our multi-disciplinary programs in Head and Neck Oncology, Neuro-Oncology, and Thoracic Oncology.

The Head and Neck Oncology Program offers a breadth of research studies including treatment of locally advanced and advanced cancers of the head and neck. In addition to providing assistance to patients suffering from neurological complications of cancer, the Neuro-Oncology program offers Phase I through II trials for patients with tumors of the nervous system, including but not restricted to brain metastases, leptomeningeal cancer, glioblastomas and less aggressive gliomas, benign brain and spinal tumors, base of brain neoplasms including pituitary disorders. Our Thoracic Oncology Program features a variety of clinical trials incorporating novel treatments for both early and advanced stage non-small cell lung cancer, as well as for other thoracic malignancies. Each program holds weekly Tumor Board meetings that provide an ideal mechanism to present challenging cases and discuss treatment options with all relevant subspecialists.

Through our ECOG Program we are able to offer studies sponsored by the National Cancer Institute. We are pleased to work with nine community hospitals/cancer treatment centers that participate in Stanford’s ECOG Community Affiliates Program. These include Community Hospital of the Monterey Peninsula, Washington Hospital in Fremont, Salinas Valley Memorial Hospital, Memorial Medical Center in Modesto, Eisenhower Medical Center in Rancho Mirage, California Cancer Care in Greenbrae, Emanual Medical Center in Turlock, Feather River Hospital in Paradise, and Santa Clara Valley Medical Center. Through these partnerships with hospitals throughout the state, Stanford is committed to providing the broadest access possible to national trials and the therapeutic advances they may offer.

We hope that you will consider a Stanford Cancer Institute clinical trial when you deem it appropriate to refer a patient to an academic medical facility. One of our many clinical trials may be an excellent option for a patient in your practice. We will make every effort to deliver great care to your patient and keep you informed of the patient’s treatment and response.

Sincerely,

Heather Wakelee, MD
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Principal Investigator, Stanford ECOG Program
Stanford Cancer Institute

RESOURCES:
Clinical Trials Recruitment Specialist
650.498.7061
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1.866.742.4811
Clinical Trials Web Search Engine
cancer.stanford.edu/trials
The Stanford Thoracic Oncology Program features a variety of clinical trials incorporating novel treatments for both early and advanced stage non-small cell lung cancer and for other thoracic malignancies. In addition, the group provides high quality standard-of-care surgical, oncological, and radiotherapeutic approaches for lung cancer patients.

**INNOVATIVE RESEARCH INCLUDES:**

- **Molecular Profiling of Lung Cancer.** Stanford Cancer Institute investigators use minute quantities of tumor tissue to tailor personalized drug therapy against certain tumors, particularly non-small cell tumors with EGFR or KRAS mutations and ALK translocations. Stanford is also correlating patients’ imaging studies with their molecular profile as part of a new field called “imageomics.”

- **Stanford physicians and basic scientists invented the MagSweeper.** This device isolates and purifies circulating cancer cells from blood, and is being used to study the genetic profiles of circulating cancer cells.

- **Stanford is at the forefront of discoveries in the Hedgehog signaling pathway.** This may yield new approaches to cancer therapy through the targeting of cancer stem cells.

- **Several mouse models of lung cancer at Stanford may lead to discoveries that can also be rapidly translated to the clinic.**

- **Advanced imaging capabilities, including clinical studies with novel PET tracers.**

**CURRENT RESEARCH HIGHLIGHTS FEATURE:**

**Early stage disease national clinical trial on chemotherapy and monoclonal antibody**

In early stage disease, Stanford is the national principal investigator for one of the highest priority national clinical cancer trials—ECOG 1505—in which patients with surgically resected non-small cell lung cancer may be treated with chemotherapy plus bevacizumab. Bevacizumab is a monoclonal antibody against vascular endothelial growth factor (VEGF), which inhibits the formation of blood vessels in tumors. It is hoped that the addition of this drug will lead to more disease cures.

**Advanced stage non-small cell lung cancer clinical trials focused on individualized treatment based on the molecular characteristics of tumors and overcoming EGFR resistance**

- **Patients with tumors with known mutations in the EGFR gene can enroll in a trial of hydroxychloroquine and erlotinib, which is designed to delay the development of resistance to erlotinib.**

- **Patients with lung cancer with KRAS mutations may be eligible for a clinical trial of another oral agent, tivantinib, and erlotinib.**

- **Two trials will soon open for patients who have previously received treatment for NSCLC.**
  - One will test the efficacy of dovitinib, which inhibits the FGF and VEGF proteins, in combination with the epidermal growth factor receptor (EGFR) inhibitor erlotinib.
  - Another will explore the mechanisms by which the oral immune stimulating agent talactoferrin may work against NSCLC.

**Studies to identify tumor cells circulating in the blood**

In collaboration with basic science colleagues, members of the Thoracic Oncology Program are participating in innovative studies evaluating two different platforms to identify tumor cells circulating in the blood. In the future, the ability to identify these cells will:

- reduce the need for invasive biopsies for patients with the disease
- allow for cutting edge testing on the cells, bringing medicine closer to the personalized treatment of lung cancer.

**Clinical outcomes research**

Stanford thoracic surgeons and oncologists are continuously reviewing their results with current and past patients to gather...
information that will help future patients. One such soon to be published study, for example, has shown that Stanford’s novel approach to patients with multifocal adenocarcinoma in situ (formerly termed bronchioloalveolar carcinoma, or “BAC”)—consisting of surgical resection of the dominant tumor and close monitoring of other smaller tumors—appears to be highly successful.

**Study of vaccine as supplement to surgery**

Also for patients with completely resected disease, the MAGRIT study evaluates immunotherapy (lung cancer “vaccine”) as a supplement to surgery. Stanford recently completed accrual for this international study, in which patients whose tumors express the MAGE-A3 tumor protein may receive immunizations against this protein after surgery. The concept of this treatment is to train the patient’s own immune system to eradicate residual tumor cells that might remain in other parts of the body even following removal of the main tumor.

**ADVANCED TECHNIQUES FOR RESECTABLE LUNG CANCER**

When a lung cancer is resectable, the Thoracic Surgery team offers advanced techniques that are available in only a few centers in the United States. These methods allow resection of the smallest amount of lung tissue that will provide the optimal chance of cure, with the least risk. They include:

- VATS (thoracoscopic) lobectomy (and VATS segmentectomy for small Stage I tumors)
- Sleeve resections to avoid pneumonectomy for centrally located tumors
- Anterior approaches to Pancoast tumors
- Endobronchial Ultrasound for biopsy of hilar and mediastinal lymph nodes
- Stereotactic Ablative Body Radiation (SABR) for stage I lung cancers in surgically ineligible or high-risk surgical patients. All patients who have a question about whether surgery or radiation therapy would be best for them are encouraged to be seen by the multidisciplinary board, which meets weekly.

**CURRENTLY OPEN STUDIES INCLUDE:**

- A Phase I Trial of Vorinostat Concurrent with Stereotactic Radiotherapy in Treatment of Brain Metastases from Non-Small Cell Lung Cancer (LUN0036)
- Phase I Study of Accelerated Hypofractionated Image-Guided Radiation Therapy (IGRT) in Patients with Stage II-IV Non-Small Cell Lung Cancer and Poor Performance Status (LUN0039)
- A Phase II Trial of Adjuvant Erlotinib in Patients with Resected, Early Stage Non-Small Cell Lung Cancer (NSCLC) with Confirmed Mutations in the Epidermal Growth Factor Receptor (EGFR) (LUN0041)
- A Phase II Study of Erlotinib with and without Hydroxychloroquine in Patients with Previously Untreated Advanced Non-Small Cell Lung Cancer and EGFR Mutations (LUN0042)
- Phase I Trial of Erlotinib and Dovitinib (TKI258) in Advanced Non-small Cell Lung Cancer (NSCLC) (LUN0044)
- A Phase II Randomized Open-Label Study of Erlotinib Plus ARQ 197 versus Single Agent Chemotherapy in Previously Treated KRAS Mutation Positive Subjects with Locally Advanced or Metastatic Non-Small Cell Lung Cancer (LUN0047)
- Phase II Trial of Individualized Lung Tumor Stereotactic Ablative Radiotherapy (SABR) (LUN0048)
- A Phase Ib Immunomodulatory Study of Single Agent Talactoferrin in Patients with Select Relapsed or Refractory Non-Small Cell Lung Cancer (NSCLC) and Squamous Head and Neck Cancer (HNSCC) (VAR0072)
- A Phase III Randomized Trial of Adjuvant Chemotherapy with or without Bevacizumab for Patients with Completely Resected Stage IB (> 4 cm)-IIA Non-Small Cell Lung Cancer (NSCLC) (ECOGE1505)
- Randomized Phase III Study of Maintenance Therapy with Bevacizumab, Pemetrexed, or a Combination of Bevacizumab and Pemetrexed Following Carboplatin, Paclitaxel and Bevacizumab for Advanced Non-Squamous NSCLC (ECOGE5508)
- A Phase II Study of L-BLP25 and Bevacizumab in Unresectable Stage IIIA and IIB Non-Squamous Non-Small Cell Lung Cancer after Definitive Chemoradiation (ECOGE6508)

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The Stanford Cancer Institute Head and Neck Oncology Program (HNOP) participates in both national and Stanford-originated clinical trials as well as translational and basic research. In addition, HNOP offers multi-disciplinary, collaborative and integrated evaluation and care for patients with head and neck cancers.

HNOP IS A PIONEER OF MAJOR SCIENTIFIC BREAKTHROUGHS THAT HELP PATIENTS THROUGH:

- Organ preservation approaches to head and neck cancer.
- New drugs for head and neck squamous cell carcinoma (HNSCC) and extending uses of existing drugs to HNSCC and nasopharyngeal carcinoma (NPC).
- Advanced radiation therapy techniques that limit toxicity and improve outcomes.
- A cutting edge method to synthesize EF5 tracer for hypoxia imaging that is now applied to patients.
- Bench to bedside approaches such as a Phase I dichloroacetate (DCA) study on modulating tumor cell activity.
- Stem cell work that extends the findings of the first paper, demonstrating the existence of “cancer stem cells” in HNSCC by researchers from Stanford and Michigan in 2007; and a 2009 Stanford study establishing that stem cell properties of patients’ malignancies correlate with prognosis.
- Normal tissue stem cell studies to identify salivary gland stem cells and to manipulate them for preservation and/or restoration of salivary gland function from radiation damage.
- HNOP’s breadth of research studies and protocols including treatment of intermediate and advanced disease as well as hypoxia imaging.
INNOVATIONS AND FEATURES AT THE HNOP INCLUDE:

- Creation of the first head and neck multidisciplinary tumor patient conference (tumor board) in the U.S.
- Introduction of the first use of chemotherapy with irradiation for head and neck squamous cell carcinoma (HNSCC), which is the basis of organ-preservation chemoradiation in the U.S.
- Close working relationships with:
  - Neurosurgery, Interventional Radiology, and Neuroradiology, which are critical for complex open and endonasal endoscopic skull base surgery
  - Endocrinology in the treatment of thyroid cancer
  - Dermatology in the treatment of advanced skin cancers.
- Innovative research by physicians now at Stanford that demonstrates the utility of the FDA-approved Mobetron for intraoperative radiation therapy.
- Contributing research in a Phase II trial of immunotherapy in intermediate and advanced surgically-treated HNSCC. A Phase III trial is now planned.
- Leadership in the head and neck disease site committee of the Radiation Therapy Oncology Group to develop new nationwide clinical trials in head and neck cancer.
- Biomarker studies to identify novel circulating biomarkers for prognostication and post-treatment surveillance in head and neck cancer.
- Strong links to developmental therapeutics such as the advancement of new drugs to treat cancer.
- Provision of a full range of treatment options that include minimally invasive surgery, robotic surgery, stereotactic radiosurgery such as CyberKnife, microvascular reconstruction, intraoperative radiation therapy (IORT), and new chemotherapy trials.

CURRENTLY OPEN STUDIES INCLUDE:

Surgery:

- A Pilot Study Assessing Transoral Robotic Surgery (TORS) for Oral and Laryngopharyngeal Benign and Malignant Lesions Using the da Vinci® Robotic Surgical System (ENT0026)

Chemotherapy, Radiation Therapy, and Chemoirradiation:

- A Phase II Study of Sequential and Concurrent Chemoradiation for Patients with Advanced Nasopharyngeal Carcinoma (NPC) (ENT0025)
- Phase I Trial of Metabolic Reprogramming Therapy for Treatment of Recurrent Head and Neck Cancers (ENT0031)
- A Feasibility Study of IMRT Modulation to Account for Scattered Radiation from Dental Fillings in Head and Neck Cancer Patients (ENT0032)
- A Phase III Randomized Trial of Chemotherapy with or without Bevacizumab in Patients with Recurrent or Metastatic Head and Neck Cancer (ECOG1305)
- A Phase III Study of Post-Operative Radiation Therapy (IMRT) +/- Cetuximab for Locally-Advanced Head and Neck Cancer (CIRB) (RTOG0920)
- A Randomized Phase II Study of Adjuvant Concurrent Radiation and Chemotherapy versus Radiation Alone in Resected High-Risk Malignant Salivary Gland Tumors (RTOG1008)
- Phase III Trial of Radiotherapy plus Cetuximab versus Chemotherapy in HPV-associated Oropharynx Cancer (RTOG1016)

Palliative Treatment:

- Weekly Docetaxel, Cisplatin, and Cetuximab (TPC) in Palliative Treatment of Patients with SCCHN (ENT0033)

• highlighted studies are Stanford investigator initiated
The Stanford Cancer Institute Neuro-Oncology Program runs national and Stanford-originated clinical trials and offers multidisciplinary, collaborative evaluation and treatment of patients with tumors of the nervous system. This includes but is not restricted to brain metastases, leptomeningeal cancer, glioblastomas and less aggressive gliomas, benign brain and spinal tumors, base of brain neoplasms including pituitary disorders, and neurological complications of cancer.

The participating faculty includes representatives from the Departments of Neurosurgery, Radiation Oncology, Neurology, Radiology, and Pathology.

**CLINICAL TRIALS HAVE FOCUSED ON:**
- vaccine therapy
- antibody therapy
- novel chemotherapy agents
- radiation sensitizers
- novel radiation therapy and radiosurgery techniques

**FEATURES OF THE ADULT NEURO-ONCOLOGY SERVICE INCLUDE:**
- Weekly Multidisciplinary Tumor Boards.
- CyberKnife stereotactic radiosurgery.
- Advanced radiation techniques such as Intensity Modulated Radiotherapy (IMRT) and Rapid Arc Volumetric Modulated Arc Therapy (VMAT).
- Expertise in base of brain surgery for tumors such as pituitary adenomas, meningiomas, acoustic neuromas, chordomas, and chondrosarcomas.
- Close working relationships between center members as well as other physicians and services within the Stanford Cancer Institute.
- Strong links to developmental therapeutics scientists within Stanford that facilitate advancement of new treatment strategies.
- Full range of treatment options including minimally invasive surgery, CyberKnife stereotactic radiosurgery, and individualized immunotherapy and chemotherapy based on molecular analysis of tumor in the Tumor Tissue Bank.
- Coordination of patient care for medical, social, and referral needs.

**CURRENTLY OPEN STUDIES INCLUDE:**
- **A Phase I/II Trial of Temozolomide and Hypofractionated Radiotherapy in Treatment of Supratentorial Glioblastoma Multiforme (BRN0012)**
- **A Phase I/II Study of Fractionated Stereotactic Radiosurgery for Large Brain Metastases (BRN0010)**
- **An International, Randomized, Double-Blind, Controlled Study of Rindopepimut/GM-CSF with Adjuvant Temozolomide for Newly Diagnosed, Surgically Resected, EGFRvIII-positive Glioblastoma (The “ACT IV” Study) (BRN0016)**
- **A Phase II Study of Rindopepimut/GM-CSF for Relapsed EGFRvIII-Positive Glioblastoma (BRN0017)**
- **A Phase I Trial of Vorinostat Concurrent with Stereotactic Radiotherapy for Brain Metastases from Non-Small Cell Lung Cancer (LUN0036)**
- **Biodistribution and Safety of the PET probes [18F]FPRGD2 and [18F]FPPRGD2 (VAR0047)**
The Stanford Cancer Institute’s Developmental Therapeutics Program, led by Branimir I. Sikic, MD, offers Phase I and II clinical trials using novel therapeutics. Dr. Sikic’s clinical interests are mainly in ovarian cancers and cancers of unknown primary. Other faculty participating in this effort include Drs. Heather Wakelee and Joel Neal (lung cancers), Dimitri Colevas (head and neck cancers), George Fisher and Pamela Kunz (GI cancers), Lauren Harshman (genitourinary cancers), Sunil Reddy (melanoma) and Ranjana Advani and Holbrook Kohrt (lymphomas).

As a translational clinical studies program, Developmental Therapeutics brings together outstanding physicians with internationally regarded scientists to develop novel therapies and diagnostic modalities that utilize cutting-edge science and technologies. This research focuses on early clinical studies, investigator-initiated trials, the development of analytic approaches to enhancing the discovery of drugs and targets, and the analysis of clinical trials.

**RESEARCH HIGHLIGHTS INCLUDE**

- Developing more effective therapies by understanding the mechanisms of resistance to anticancer drugs, particularly multidrug resistance (MDR1/P-glycoprotein), resistance to taxanes, and pharmacogenetics and pharmacogenomics.
- Running laboratory projects that study drug transporters, taxane resistance mechanisms including tubulin gene expression and epithelial to mesenchymal transition, and pharmacogenetic and genomic studies related to clinical trials in ovarian cancer, colorectal cancers, and pediatric leukemias.
- Investigating the prognostic significance of resistance gene expression in cancer.
- Directing Phase I and II trials of new tyrosine kinase inhibitors both as single agents and integrated with standard chemotherapies.
- Engaging in translational studies of molecular determinants of therapeutic response and toxicity.
- Developing novel immunotherapies for lymphomas.

Below is a sampling of currently available Phase 1 and 2 studies.

**PHASE 1 STUDY**

**Lymphomas**

- A Phase I Trial of an Anti-CD22 Monoclonal Antibody Conjugate

**PHASE 2 STUDIES**

**Thymic Cancers**

- A Phase 2 Study of Amrubicin in Relapsed or Refractory Thymic Malignancies (THOR0003)

**Mantle Cell and Diffuse Large B-Cell Lymphomas**

- Multicenter Phase 2 Study of Bruton’s Tyrosine Kinase (Btk) Inhibitor, PCI-32765, in Relapsed or Refractory Mantle Cell Lymphoma (LYMNHL0084)
- A Multicenter, Open-Label, Phase 2, Safety and Efficacy Study of the Bruton’s Tyrosine Kinase (Btk) Inhibitor, PCI-32765, in Subjects with Relapsed or Refractory de novo Diffuse Large B-cell Lymphoma (DLBCL) (LYMNHL0088)

**Gastric Cancers**

- A Phase 2 Study of Capecitabine, Carboplatin, and Bevacizumab for Metastatic or Unresectable Gastroesophageal Junction and Gastric Adenocarcinoma (GI0002)
THORACIC ONCOLOGY PROGRAM
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- A Randomized Phase III Study of Sublobar Resection (+/- Brachytherapy) versus Stereotactic Body Radiation Therapy in High Risk Patients with Stage I Non-Small Cell Lung Cancer (NSCLC) (ACOSOGZ4099)
- Phase III Comparison of Thoracic Radiotherapy Regimens in Patients with Limited Small Cell Lung Cancer also Receiving Cisplatin and Etoposide (RTOG0538)
- Randomized Phase II Study of Pre-Operative Chemoradiotherapy +/- Panitumumab (IND #110152) Followed by Consolidation Chemotherapy in Potentially Operable Locally Advanced (Stage IIIA, N2+) Non-Small Cell Lung Cancer (RTOG0839)

ADULT NEURO-ONCOLOGY GROUP
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- Effect of the Novel Somatostatin Analog Pasireotide in Rare Tumors of Neuroendocrine Origin (ENDO010)
- A Phase II Trial of Hippocampal Avoidance during Whole Brain Radiotherapy for Brain Metastases--RTOG CCOP Study (RTOG0933)
- Phase II/III Study of Image-guided Radiosurgery/SBRT for Localized Spine Metastasis (RTOG0631)

RESOURCES:
Clinical Trials Recruitment Specialist
650.498.7061
Referral Center
1.866.742.4811
Clinical Trials Web Search Engine
cancer.stanford.edu/trials