Welcome to the premier issue of the Stanford Cancer Center Clinical Research Newsletter! This quarterly publication is designed to inform our colleagues in the medical community, and especially physicians who are considering treatment options for their patients with cancer, about current clinical trials and research studies available at the NCI-designated Stanford Cancer Center. In each issue we will highlight the clinical trials and novel treatments offered in three specific disease areas. In addition, we will also present some early-phase clinical trials from our Developmental Therapeutics Program.

Stanford Cancer Center physicians are engaged in a broad spectrum of more than 300 clinical trials and research studies. Most evaluate the effectiveness of new cancer therapies, including new chemotherapies and drug modifiers, innovative radiotherapeutic approaches, monoclonal antibodies, biologics, vaccines, and multidisciplinary treatments. Along with our own physician-led studies, which are unique to Stanford, we offer NCI Cooperative Group and industry sponsored trials. One of our many clinical trials may be the best treatment choice for your patient, especially for those with advanced stage disease, recurrent cancers, and cancers that are difficult to cure.

This issue is devoted to telling you about our multi-disciplinary programs in Head and Neck Oncology, Thoracic Oncology, and Neuro-Oncology. The Head and Neck Oncology Program created the first head and neck multidisciplinary tumor board in the U.S., and has been a pioneer in introducing the first use of chemotherapy with irradiation for head and neck squamous cell carcinoma. The Thoracic Oncology Program features a wide number and 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. Our Neuro-Oncology program offers Phase I and II trials for patients with malignancies of the nervous system including brain metastasis, as well as leptomeningeal cancer, glioblastomas and less aggressive gliomas, base of brain neoplasms including pituitary disorders, and neurological complications of cancer.

We hope that you will consider a Stanford Cancer Center clinical trial when you deem it appropriate to refer a patient to an academic medical facility. We, in turn, will make every effort to deliver great care to your patient, keep you informed of the patient’s treatment and response, and if clinical trial treatment is not appropriate for your patient, return them to your care.

Beverly S. Mitchell, MD
George E. Becker Professor of Medicine
Director, Stanford Cancer Center
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:
  1. Neurosurgery, Interventional Radiology, and Neuroangiography, which are critical for complex open and endonasal endoscopic skull base surgery
  2. Endocrinology in the treatment of thyroid cancer
  3. 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 I trial of immunotherapy in intermediate and advanced surgically-treated HNSCC. A Phase II trial is now planned.
- 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.

HNOP is a pioneer of major scientific breakthroughs that help patients through:

- Organ preservation approaches to head and neck cancer.
- New drugs for 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.
- HNOP’s breadth of research studies and protocols include treatment of intermediate and advanced disease as well as hypoxia imaging.

TREATMENT 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)
- A Phase II, Open-label Trial of the Safety & Biological Effect of Pre-operative Peri-lymphatic Ultralow Dose IrX-2 (with Cyclophosphamide, Indomethacin, and Zinc) in Patients with Resectable Cancer of the Head and Neck: A Study of a Role of Immunotherapy in HNSCC (ENT0018)
- A Pilot Study Assessing Transoral Robotic Surgery for Oral and Laryngopharyngeal Benign and Malignant Lesions Using the da Vinci® Robotic Surgical System (ENT0026)

Chemotherapy, Radiation Therapy, and Chemoirradiation:
- A Multi-Institutional Phase II Study of Radiation and GW572016 Creation of the first head and neck multidisciplinary tumor patient conference (tumor board) in the U.S.
- A Phase II Trial of Induction Chemotherapy Followed by Cetuximab (Erbitux) with Low Dose vs. Standard Dose IMRT in Patients with HPV-Associated Resectable Squamous Cell Carcinoma of the Oropharynx (ECOG1308)
- A Phase III Study of Post-Operative Radiation Therapy (IMRT) +/- Cetuximab for Locally-Advanced Head and Neck Cancer (CRB) (RT060920)
- A Phase I Dose Escalation Study of OMP-21M18 in Subjects with Solid Tumors (VAR0039)

Thyroid Cancer:
- An International, Randomized, Double-Blinded, Phase III Efficacy Study of XL184 versus Placebo in Subjects with Unresectable, Locally Advanced, or Metastatic Medullary Thyroid Cancer (END0006)
- A Double-Blind, Randomized Phase III Study Evaluating the Efficacy and Safety of Sorafenib Compared to Placebo in Locally Advanced/Metastatic RAI-Refractory Differentiated Thyroid Cancer (END0009)

The Stanford Cancer Center Head and Neck Oncology Program (HNOP) offers multi-disciplinary, collaborative and integrated evaluation and care for patients with head and neck cancers. The faculty is well known and respected and participates in both national and Stanford-originated clinical trials as well as translational and basic research.
The Stanford Thoracic Oncology group features a wide number and variety of clinical trials incorporating novel treatments for both early and advanced stage non-small cell lung cancer and for other thoracic malignancies.

**ADVANCED TECHNIQUES FOR RESECTABLE LUNG CANCER**

When a lung cancer is resectable, the thoracic surgery group led by Joseph Shrager, MD, offers advanced techniques not widely available. These techniques include:

- VATS thoracoscopic lobectomy.
- Sleeve resections to avoid pneumonectomy, and
- Segmentectomy for small, stage IA tumors.

Stanford thoracic surgeons directly participate in stereotactic radiotherapy treatments for lung cancer. This enables them to provide an unbiased assessment of whether surgery, or this emerging form of treatment for small lung cancers, is most appropriate for an individual patient.

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

In early stage disease, Stanford oncologist Dr. Heather Wakelee 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.

**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. Patients whose tumors express the MAGE-A3 tumor protein are given 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 stage non-small cell lung cancer clinical trials focused on individualized treatment and overcoming EGFR resistance**

For advanced stage non-small cell lung cancer, Stanford is conducting clinical trials to individualize treatment based on the molecular characteristics of tumors. For patients with tumors expressing the ALK protein, ongoing studies are investigating the efficacy of crizotinib (PF-02341066), a small molecule that specifically inhibits ALK tyrosine kinase. In early phase clinical studies using this drug, over two-thirds of patients had a significant reduction in the size of tumors. An additional clinical trial is testing the efficacy of another small molecule, XL-184, which inhibits the MET and VEGF proteins, in combination with the epidermal growth factor receptor (EGFR) inhibitor erlotinib. The purpose of the trial is to help patients overcome resistance to erlotinib therapy, which is now recognized as a major clinical problem. Numerous additional studies are soon to open that explore multiple strategies to overcome EGFR resistance.

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

In collaboration with basic science colleagues, members of the Thoracic Oncology group 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.

**TREATMENT STUDIES INCLUDE:**

**Lung:**

- A Phase I Trial of Vorinostat Concurrent with Stereotactic Radiotherapy in Treatment of Brain Metastases from Non-Small Cell Lung Cancer (LUN0036)
- A Phase I/II Study of XL184 with or without Erlotinib in Subjects with Non-Small Cell Lung Cancer (LUN0027)
- A Phase I/II Study of Albriccept Administered in Combination with Pemetrexed and Cisplatin in Patients with Advanced Carcinoma (LUN0028)
- International Randomized Study to Compare CyberKnife® Stereotactic Radiotherapy with Surgical Resection in Stage I Non-small Cell Lung Cancer (LUN0029)
- A Double-blind, Randomized, Placebo-Controlled Phase III Study to Assess the Efficacy of recombMAGE-A3 + AS15 Antigen-Specific Cancer Immunotherapeutic as Adjuvant Therapy in Patients with Resectable MAGE-A3-positive Non-Small Cell Lung Cancer (LUN0030)
- A Phase III, Multi-center, Placebo-controlled Trial of Sorafenib (BAY 43-9006) in Patients with Relapsed or Refractory Advanced Predominantly Non Squamous Non-Small Cell Lung Cancer (NSCLC) after 2 or 3 Previous Treatment Regimens (LUN0035)

- Phase III, Randomized, Open-Study of the Efficacy and Safety of PF-2341066 versus Standards of Care Chemotherapy (Pemetrexed or Docetaxel) in Patients with Advanced Non-small Cell Lung Cancer (NSCLC) Harboring a Translocation or Inversion Event Involving the Anaplastic Lymphoma Kinase (ALK) Gene Locus (LUN0037)

- A Phase II, Open-label Single Arm Study of the Efficacy and Safety of PF-2341066 in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) Harboring a Translocation or Inversion Involving the Anaplastic Lymphoma Kinase (ALK) Gene Locus (LUN0038)

- A Phase III Randomized Trial of Adjuvant Chemotherapy with or without Bevacizumab for Patients with Completely Resected Stage IB (N = 4 cm) - IIA Non-Small Cell Lung Cancer (NSCLC) (ECOGE1505)

- A Randomized Phase II Study of Cisplatin and Etoposide in Combination with Either Hedgehog Inhibitor GD-0449 or IG-F-IR MoAB/IMC-A12 for Patients with Extensive Stage Small Cell Lung Cancer (ECOGE1508)

- Three-Arm Randomized Phase II Study of Carboplatin and Paclitaxel in Combination with Cetuximab, IMC-A12 or Both for Advanced Non-small Cell Lung Cancer Patients Who Will Not Receive Bevacizumab-based Therapy (ECOGE4508)

- A Phase III Randomized Trial of Lobectomy versus Sublobar Resection for Small (<=2 cm) Peripheral Non-small Cell Lung Cancer (ACOSOG/CA1B140503)

- Phase III Comparison of Thoracic Radiotherapy Regimens in Patients with Limited Small Cell Lung Cancer also Receiving Cisplatin and Etoposide (RTOG0638)

- A Randomized Phase II Comparison of Standard-dose (60 Gy) versus High-dose (74 Gy) Conformal Radiotherapy with Concurrent and Consolidation Carboplatin/Paclitaxel +/- Cetuximab (NID # 103444) in Patients with Stage IIA/IIB Non-small Cell Lung Cancer (RTOG0617)

- A Randomized Phase II Study Comparing 2 Stereotactic Body Radiation Therapy (SBRT) Schedules for Medically Inoperable Patients with Stage I Peripheral Non-Small Cell Lung Cancer (RTOG0915)

**CLINICAL TRIALS RECRUITMENT SPECIALIST**

650.498.7061
cancer.stanford.edu/trials
Adult Neuro-Oncology Disease Management Group
Multidisciplinary, Collaborative Approaches for Evaluation and Treatment of Nervous System Cancers

The Stanford Cancer Center Neuro-Oncology program offers a multidisciplinary, collaborative approach for evaluation and treatment of patients with malignancies of the nervous system. This includes but is not restricted to brain metastases, leptomeningeal cancer, glioblastomas and less aggressive gliomas, 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.

FEATURES OF THE ADULT NEURO-ONCOLOGY SERVICE:
- Weekly Multidisciplinary Tumor Boards.
- Cyberknife radiotherapy.
- Expertise in base of brain surgery including chordomas, chondrosarcomas, and pituitary adenomas.
- Close working relationships between members as well as other physicians and services within the Cancer Center.
- Strong links to developmental therapeutics within Stanford so that new treatment strategies can be advanced.
- Provision of a full range of treatment options to include minimally invasive surgery, CyberKnife, and Tissue Banking.

ONGOING CLINICAL TRIALS 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 to Treat Large Brain Metastases (BRN0010)
- A Phase I Trial of Vorinostat Concurrent with Stereotactic Radiotherapy in Treatment of Brain Metastases from Non-Small Cell Lung Cancer (LLN0036)
- Biodistribution and Safety of the PET probes [18F]FPRGD2 and [18F]FPPRGD2 (VAR0047)
- Phase II Study of Azixa™ (MPC-6827) for the Treatment of Patients with Recurrent Glioblastoma Multiforme (BRN0009)
- Effect of the Novel Somatostatin Analog Pasireotide in Rare Tumors of Neuroendocrine Origin (END0010)
- Phase II/Ill Study of Image-guided Radiosurgery/SBRT for Localized Spine Metastasis (RTOG0231)

• highlighted studies are Stanford investigator initiated
Stanford Cancer Center’s Developmental Therapeutics Program, led by Branimir Sikic, MD, offers early-phase clinical trials using novel therapeutics. Phase I studies are aimed at advanced cancers. Below is a sampling of currently available Phase I studies.

**PHASE 1 STUDIES – MULTIPLE SITES**

### Any Site
- A Phase I Dose Escalation Study to Evaluate the Safety and Tolerability of HGS1029 (AEG40826•2HCl) in Patients with Advanced Solid Tumors (VAR0031)
- A Phase I Dose Escalation Study of OMP-21M18 in Subjects with Solid Tumors (VAR0039)

### Hematologic Cancers
- **Chronic Lymphocytic Leukemia (CLL)**
- **B-Cell Non-Hodgkin Lymphoma (NHL)**
- A Phase I Study to Investigate the Safety and Clinical Activity of CAL-101 in Combination with Bendamustine and Rituximab in Patients with Relapsed or Refractory Indolent B-cell Non-Hodgkin’s Lymphoma or Chronic Lymphocytic Leukemia (HEM0017)

### Prostate and Ovarian Cancers
- A Randomized Discontinuation Study of XL184 in Subjects with Advanced Solid Tumors (VAR0046)

### Skin Cancer
- **Basal Cell Carcinoma**
- A Phase I Study of IPI-926 in Patients with Advanced and/or Metastatic Solid Tumor Malignancies (SKIN0005)

**RESOURCES:**
- Clinical Trials Recruitment Specialist
  650.498.7061
- Referral Center
  650.498.6000
- Clinical Trials Web-based Search Engine
  cancer.stanford.edu/trials