Welcome to the Summer 2012 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 Stanford Cancer Center. We have more than 300 clinical trials open for cancer patients. Along with our own physician-led studies, which are unique to Stanford, we offer NCI Cooperative Group and selected industry sponsored trials. Many of these trials provide access to novel therapies including new “targeted” agents, often not available in the community.

In each issue we highlight a number of trials and novel treatments by focusing on three different disease areas. The newsletter concludes with some of our promising early-phase clinical trials. As the co-leader of the Gastrointestinal Oncology Program and the Medical Director of our Clinical Trials Office, I am pleased to introduce our multi-disciplinary programs in Gastrointestinal (GI) Oncology, Cutaneous Oncology, and Sarcoma. Each program offers weekly Tumor Boards. These provide an ideal mechanism to present challenging cases and discuss treatment options with all relevant subspecialists.

The Gastrointestinal Oncology Program conducts studies on many promising new agents, as well as offering advanced radiation therapy, minimally invasive laparoscopic and robotic surgeries. Of particular interest is a randomized vaccine study of resected pancreas cancer. For patients with unresectable pancreas cancer, Stanford is leading a multicenter trial with Memorial Sloan Kettering and Johns Hopkins investigating the role of stereotactic radiosurgery. For these studies, the local oncologist can administer standard chemotherapy.

The Cutaneous Oncology Program features a wide number and variety of clinical trials. The program offers innovative melanoma prevention and treatment trials, novel therapies for invasive basal cell carcinoma, and has recently expanded its clinical programs in high-risk squamous cell carcinoma, merkel cell carcinoma, and supportive dermato-oncology.

The Sarcoma Program’s clinical trials focus on targeted therapies and newer drugs such as denosumab and nilotinib. The program includes interventional radiology services, stereotactic body radiation therapy, and intraoperative radiotherapy. We are an active participant in the Sarcoma Alliance for Research through Collaboration (SARC) and offer a variety of SARC trials, along with trials conducted in collaboration with Dana Farber Cancer Institute and MD Anderson Sarcoma Center.

We hope that you will consider Stanford Cancer Center for your patients who might be appropriate for clinical trials or multidisciplinary consultation. 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.

George A. Fisher, MD, PhD
Associate Professor of Medicine
Medical Director, Cancer Clinical Trials Office
Stanford's Gastrointestinal (GI) Oncology Program integrates the latest laboratory discoveries, technological innovations, and support services into the care of cancer patients. As an NCI designated cancer center, Stanford is renowned for its contributions to cancer research and for the translation of research successes to the benefit of patients. Specialists work together to develop a personalized treatment strategy that offers the best chance of a favorable outcome, aiming for cure whenever possible.

GI ONCOLOGY MULTIDISCIPLINARY TEAM OF SPECIALISTS
This multidisciplinary team consists of specialists who focus on cancers of the GI tract. These include cancers of the esophagus, stomach, liver, pancreas, bile duct, gall bladder, small intestine, appendix, colon, rectum, and anus. In addition, rare tumors such as neuroendocrine (carcinoid), GI Stromal Tumors (GIST), and pseudomyxoma peritonei fall within the GI Oncology Program domain.

Team members work under one roof enabling seamless transitions among specialties and often same-day appointments with cancer surgeons, radiation oncologists, and medical oncologists. The GI Oncology Program also meets weekly with interventional and diagnostic radiologists, nuclear medicine specialists, gastroenterologists, and pathologists to review complex cases and newly diagnosed patients who would benefit from multidisciplinary expertise.

KEY ATTRIBUTES OF THE GI ONCOLOGY PROGRAM:
World Renowned Expertise in Radiation Oncology: Stanford is the birthplace of modern radiation therapy with contributions such as the first linear accelerator and the first CyberKnife. SCC also has the first Trilogy and TrueBeam systems for clinical use in the Western U.S. Many of the stereotactic radiotherapy techniques used routinely around the world were developed here. The first clinical trials investigating single fraction stereotactic body radiotherapy (SBRT) or stereotactic ablative radiotherapy (SABR) in liver and pancreas were from Stanford. GI radiation oncologists continue to improve the precision with which they radiate tumors while sparing adjacent normal tissues.

Minimally Invasive Laparoscopic and Robotic Surgeries: Specialists in surgical oncology can sometimes remove cancers using a laparoscope, which can result in equally successful outcomes while limiting the size of the incision (and scar) and improving the recovery time following surgery. Surgeons offer laparoscopic procedures routinely for colon cancer and for selected cancers involving the stomach, pancreas, liver, and rectum. For selected patients with rectal cancer, Stanford can now offer “robotic” surgeries, a technological innovation that has been proven to be successful for prostate cancer and is now being applied to rectal cancers.
State of the Art Imaging Modalities and Regional Therapies: GI diagnostic and interventional radiologists as well as nuclear medicine specialists collaborate to provide the highest resolution images of tumors. Identifying the full anatomic extent of an individual cancer is key to determining the optimal treatment of the patient. For example, for selected patients whose cancer is limited to the liver, interventional radiologists can administer treatments directly through the blood vessels that feed the tumors in the liver, thus minimizing side effects of drugs to the rest of the body. Furthermore, high resolution MRIs determine which rectal cancer patients might benefit from radiation and which ones might be able to avoid a colostomy.

Weekly GI and Liver Tumor Boards: Newly diagnosed patients with GI cancers who might benefit from multidisciplinary consultation are seen in the weekly GI Tumor Board or in the weekly Liver Tumor Board. Anyone with localized pancreas, gastric, or rectal cancer may bring their family or close friends to a tumor board appointment where the entire GI Tumor Board reviews their medical history, pathology, and radiographic studies followed by a face-to-face discussion and consultation with the cancer surgeon, the medical oncologist, and the radiation oncologist. The advantage of meeting all relevant subspecialists to address patient and family questions and concerns is a unique feature of the tumor boards and an immense source of satisfaction for patients and their families.

Access to Novel Therapies: GI specific medical oncologists conduct studies on the most promising drugs that come from laboratory experimentation. For instance, drugs that are now standard for patients with colorectal cancer were available in clinical trials at Stanford and other cancer centers years before they were approved. Centers such as Stanford are poised to lead the field of new targeted therapeutics specifically suited to the molecular features of an individual’s tumor, thereby ushering in the era of true personalized oncology care.

TRIALS OF PARTICULAR INTEREST:
• Randomized vaccine study of resected pancreas cancer in which the standard chemotherapy or chemoradiation can be administered by the patient’s local oncologists.
• Multicenter trial led by Stanford with Memorial Sloan Kettering and Johns Hopkins that is investigating the role of stereotactic radiosurgery for unresectable pancreas cancer. Again, the standard “chemo” can be administered by the patient’s local oncologist.
• Phase II trials using targeted agents for newly diagnosed metastatic colorectal, gastro-esophageal and pancreas cancers, and chemo-radiation for localized cholangiocarcinomas, anal cancers as well as trials for carcinoid syndrome and metastatic neuroendocrine tumors.

The Stanford GI Oncology Program feels that there are no “simple” GI cancers and that each newly diagnosed patient deserves the expertise that only a multidisciplinary team of GI-focused specialists can bring to bear. The best time to cure a cancer is the first time.

CLINICAL STUDIES INCLUDE:
Cholangiocarcinoma:
• A Phase II Trial of Adjuvant Capecitabine/Gemcitabine Chemotherapy Followed by Concurrent Capecitabine and Radiotherapy in Extrahepatic Cholangiocarcinoma (EHCC) (SWOGS0809)
• Phase II Study of Stereotactic Body Radiotherapy (SBRT) and Chemotherapy for Unresectable Cholangiocarcinoma Followed by Liver Transplantation (HEP0032)

**Colon & Rectum Cancer:**
- A Phase 2 Randomized, Double-Blinded, Placebo-Controlled Study to Evaluate the Efficacy and Safety of GS-6624 Combined with FOLFIRI as Second Line Treatment for Metastatic KRAS or BRAF Mutant Colorectal Adenocarcinoma that Has Progressed Following a First Line Oxaliplatin- and Fluoropyrimidine-Containing Regimen (COR0010) (Soon to Open)
- Statin Polyp Prevention Trial in Patients with Resected Colon Cancer (NSABPP5)

**Gastroesophageal Adenocarcinoma:**
- **FIRST LINE METASTATIC DISEASE:** A Phase II Study of Capecitabine, Carboplatin, and Bevacizumab for Metastatic or Unresectable Gastroesophageal Junction and Gastric Adenocarcinoma (GI0002)
- **SECOND LINE METASTATIC DISEASE:** Randomized Phase II Study of Paclitaxel with or without the Anti-IGF-IR mAb Cixutumumab (IMC-A12) as Second Line Treatment for Patients with Metastatic Esophageal or GE Junction Cancer (ECOGE2208)
- A Phase III Trial Evaluating the Addition of Cetuximab to Paclitaxel, Cisplatin, and Radiation for Patients with Esophageal Cancer who are Treated without Surgery (RTOG0436)
- A Phase III Trial Evaluating the Addition of Trastuzumab to Trimodality Treatment of Her2-Overexpressing Esophageal Adenocarcinoma (RTOG1010)

**GI Stromal Tumors**
- A Phase II Study of Pazopanib in Patients with Imatinib Refractory or Intolerant Gastrointestinal Stromal Tumors (GIST) (GIST0003)

**Liver Cancer:**
- Phase II Study of Combination Stereotactic Body Radiotherapy (SBRT) with Transarterial Chemo-Embolization (TACE) for Unresectable Hepatocellular Carcinoma (HEP0024)
- A Randomized, Double-blind, Multicenter Phase III Study of Brivanib versus Placebo as Adjuvant Therapy to Trans-Arterial Chemo-Embolization (TACE) in Patients with Unresectable Hepatocellular Carcinoma: The BRISK TA Study (HEP0025)
- A Phase III Randomized, Double-Blind Trial of Chemoembolization with or without Sorafenib in Unresectable Hepatocellular Carcinoma (HCC) in Patients with and without Vascular Invasion (ECOGE1208)

**Neuroendocrine Tumors:**
- A Double-blind, Randomized Placebo-controlled Clinical Trial Investigating the Efficacy and Safety of Somatuline Depot (lanreotide) Injection in the Treatment of Carcinoid Syndrome (END0007)
- An Open Label, Multicenter, Single Arm Study of Pasireotide LAR in Patients with Rare Tumors of Neuroendocrine Origin (CSOM230D2203) (END0010)
- A Phase II Study of Capecitabine, Temozolomide and Bevacizumab for Metastatic or Unresectable Pancreatic Neuroendocrine Tumors (END0012) (Soon to Open)
- Phase II Study of Pasireotide LAR in Patients with Metastatic Neuroendocrine Carcinomas (END0013)
- Phase III Prospective Randomized Comparison of Depot Octreotide Plus Interferon Alpha versus Depot Octreotide Plus Bevacizumab (NSC #704865) in Advanced, Poor Prognosis Carcinoid Patients (ECOGS0518)
- Randomized Phase II Study of Everolimus Alone Versus Everolimus Plus Bevacizumab in Patients With Locally Advanced or Metastatic Pancreatic Neuroendocrine Tumors (ECOGC80701)

**Pancreas Cancer:**
- A Phase III Study of Chemotherapy and Chemoradiotherapy with or without HyperAcute®-Pancreatic Cancer Vaccine in Subjects with Surgically Resected Pancreatic Cancer (PANC0011)
- A Phase II Multi-Institutional Study to Evaluate the Efficacy of Gemcitabine and Fractionated Stereotactic Radiotherapy for Unresectable Pancreatic Adenocarcinoma (PANC0007)
- A Phase 2 Randomized, Double-Blinded, Placebo-Controlled Study to Evaluate the Efficacy and Safety of GS-6624 Combined with Gemcitabine as First Line Treatment for Metastatic Pancreatic Adenocarcinoma (PANC0013) (Soon to Open)
- A Phase II Study of L-BLP25 and Bevacizumab in Unresectable Stage IIIA and IIIB Non-Squamous Non-Small Cell Lung Cancer after Definitive Chemoradiation (ECOGE6508)
Developmental Therapeutics
Phase 1 and 2 Studies for Multiple Cancers

Stanford Cancer Center’s Developmental Therapeutics Group, led by Branimir I. Sikic, MD, offers Phase 1 and 2 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), Mark Pegram and Melinda Telli (breast 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
• 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.
• 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 and other cancers.

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 DCDT2980S in Relapsed or Refractory B-Cell Non-Hodgkin’s Lymphomas (VAR0059)
• A Phase I Study of PF-05082566 as a Single Agent in Patients with Advanced Cancer, and in Combination with Rituximab in Patients with Non-Hodgkin’s Lymphoma (NHL) (LYMNHL0092)
• A Phase I Study of the Safety, Tolerability, Pharmacokinetics and Immunoregulatory Activity of BMS-663513 (Anti-CD137) in Subjects with Advanced and/or Metastatic Solid Tumors (VAR0071)

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
• 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)

• highlighted studies are Stanford investigator initiated
The **Skin Cancer Program** at the Stanford Cancer Institute is a leading innovator in the research and treatment of skin cancer, including melanoma, basal cell carcinoma, squamous cell carcinoma, Merkel cell carcinoma, and cutaneous lymphoma. The Stanford Pigmented Lesion and Melanoma Program (PLMP) is a recognized leader in primary and secondary prevention research, including chemoprevention studies and early detection strategies to enhance the likelihood of cure. Under the direction of Radiation Oncologist Susan Knox, MD, PhD, Stanford is leading a novel trial of ipilimumab in conjunction with palliative radiation therapy for metastatic melanoma patients. This study will test whether ipilimumab combined with radiation therapy enhances the body’s ability to attack melanoma—even outside of the radiation field.

The Stanford PLMP is directed by Susan M. Swetter, MD, Professor of Dermatology, Stanford University Medical Center & Cancer Institute and VA Palo Alto Health Care System. Dr. Swetter has just received the 2012 Humanitarian Award from the Melanoma Research Foundation. In addition, she has published three papers in the journal *Cancer* this year regarding 1) the importance of physician skin examination in promoting thinner melanoma detection in older men, who are more likely to develop and die from melanoma; 2) the adverse effect of lower education and socioeconomic status on physician-patient communication, melanoma awareness, and performance of physician skin examination; and 3) results of a phase II study assessing the potential chemopreventive activity of sulindac, a nonsteroidal anti-inflammatory agent in patients at increased risk of melanoma.

**Expansion in the Cutaneous Malignancies Dermatology and Surgical Teams.** Stanford welcomed Clinical Associate Professor Sumaira Aasi, MD to the Dermatology faculty in 2011 as Director of Mohs and Dermatologic Surgery at the Stanford Medicine Outpatient Center. Dr. Aasi previously served as Associate Chief of the Section of Dermatologic Surgery and Cutaneous Oncology at Yale University. Her clinical and research interests include non-melanoma skin cancer, high-risk skin cancer, histology and surgical reconstruction. Clinical Assistant Professor Michael Krathen, MD joined the Dermatology faculty and cutaneous lymphoma and melanoma teams in 2011. Dr. Krathen will be concentrating his efforts in the cutaneous lymphoma realm and has initiated a new Post-Transplant / High Risk Skin Cancer Clinic in Stanford Dermatology, which focuses on patients who are
at a high risk of developing skin cancer (especially squamous cell carcinoma) due to various causes, including immune suppression therapy following a solid organ transplant. Dr. Krathen will also spearhead development of a Multidisciplinary Merkel Cell Carcinoma Program within the SCC in conjunction with surgical and medical oncology colleagues. Dr. Bernice Kwong will be joining the Dermatology and Cancer Center faculty in the fall of 2012 to develop a novel Supportive Dermato-Oncology Program within the Stanford Cancer Center (SCC), which will enhance dermatologic assessment and treatment of known side effects and complications of cancer treatment, including skin manifestations of graft versus host disease in patients who have undergone bone marrow transplantation.

Stanford was fortunate to recruit Head and Neck surgeon, John Sunwoo, MD, to the PLMP in June 2011. Dr. Sunwoo is Assistant Professor of Otolaryngology (Head and Neck Surgery). One of his main clinical interests is melanoma of the head and neck, and his research interests include the study of natural killer cells and the immune response to cancer stem cells to improve understanding of host immune surveillance in malignant transformation and cancer development. Dr. Vasu Divi will be joining the Stanford Otolaryngology Head and Neck Surgery Program as Assistant Professor this year and will be working along with Dr. Sunwoo for management of head and neck melanoma and Merkel cell carcinoma cases.

Collaborative Surgical Team Expands, Performs Sentinel Lymph Node (SLN) Biopsy for Melanoma Staging and Resection of Advanced Disease and Research to Improve Skin Cancer Surgery. Stanford surgeons (dermatology, head and neck surgery, general surgery/surgical oncology) perform surgery for all stages of melanoma, from early disease to the most advanced. Dermatologic surgeons operate on patients with melanoma in situ and thinner tumors that do not require simultaneous staging with the sentinel lymph node biopsy procedure. Surgical Oncologists specialize in melanoma surgery for patients with head and neck tumors (Otolaryngology, Head & Neck Surgery) or for melanoma elsewhere on the body (General Surgery/Surgical Oncology).

The Stanford PLMP features a collaborative team of melanoma surgeons who perform sentinel lymph node biopsy (SLNB) for melanoma staging, as well as resection of more advanced disease. The Skin Cancer Program uses SLNB to detect microscopic spread of melanoma and Merkel cell carcinoma in regional lymph nodes with novel imaging modalities to improve accuracy. Significant advances in localizing sentinel lymph nodes have occurred over the years, and the Stanford melanoma surgeons work closely with the Stanford Division of Nuclear Medicine and Molecular Imaging during the preoperative assessment and lymphatic mapping. Newer imaging techniques, such as SPECT/CT, have dramatically improved Stanford surgeons’ ability to assess the location of the sentinel lymph node in the setting of complex anatomy. Novel devices to help facilitate the intraoperative localization of sentinel nodes are also being developed at Stanford and tested in conjunction with members of the Radiology and Engineering Departments. One such device that is currently under investigation is a handheld gamma camera, developed in the Molecular Imaging Program at Stanford, that allows for real-time spatial imaging of the sentinel lymph nodes containing the radioactive tracer.
MELANOMA CLINICAL-EPIEMIOLOGICAL RESEARCH: Cancer Prevention Institute of California Collaborative Projects. The Stanford PLMP enjoys a longstanding collaboration with senior epidemiologist Christina Clarke-Dur, PhD, at the Cancer Prevention Institute of California and other renowned epidemiologists to develop greater understanding of melanoma incidence and mortality among individuals with different racial-ethnic and socioeconomic backgrounds. In 2011, Drs. Clark-Dur and Swetter published an article demonstrating 80% increased melanoma incidence in young white women (aged 15-39) in California who resided in neighborhoods with highest socioeconomic status (SES) and ultraviolet radiation (UVR) exposure compared with those in the lowest categories. These trends were not observed in women living in low SES/high UVR areas, suggesting that affluence, and associated lifestyle behaviors such as indoor tanning, may have a greater impact on melanoma risk that UVR exposure alone. This study was heralded for its effect on passage of SB 746 in 2011, which banned access of minors to tanning beds in the state of California.

MELANOMA TRANSLATIONAL RESEARCH HIGHLIGHTS: Stem Cell and Molecular Research. Stanford melanoma team members continue to collaborate in the area of stem cell research with Irving Weissman, MD, Director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine. In human melanoma, Dr. Weissman’s group has found that stem cells express a certain neural crest nerve growth factor receptor (CD271) against which immunotherapies and other agents might eventually be tested. Identification of genetic alterations and pathways of melanoma development are also in progress in the laboratory of Dr. Paul Khavari, Professor and Chair of Dermatology and will provide powerful therapeutic options for patients diagnosed with all stages of melanoma.

STANFORD UNIVERSITY MEDICAL CENTER DERMATOPATHOLOGY SERVICES Expert Pathology Diagnosis. Stanford Dermatopathology Program dermatopathologists [Jinah Kim, MD, PhD (Assistant Professor of Pathology & Dermatology, Director, Dermatopathology Service); Uma Sundram, MD, PhD (Assistant Professor of Pathology & Dermatology), Britney DeClerk, MD (Clinical Assistant Professor of Dermatology & Pathology), and Kerri Rieger, MD, PhD (Clinical Assistant Professor of Dermatology & Pathology) are specially trained to study skin samples and have expertise in the diagnosis of pigmented lesion pathology.

Advanced Molecular Studies SNaPshot genotyping. Much of current cancer therapy is targeted against specific genetic mutations in cancer cells and signaling pathways. This requires the rapid and accurate identification of genetic abnormalities that can predict a patient’s response to a specific medication. Stanford Dermatopathology utilizes a highly-sensitive clinical test to identify several of the most common genetic changes that cause melanoma, and for which some targeted therapies are now available. Testing is performed directly on the skin samples obtained for diagnosis. The mutations that Stanford currently tests include: BRAF V600E, BRAF V600M, NRAS Q61L, and NRAS Q61R.

Maligna FISH (Fluorescent In Situ Hybridization) Assay. Stanford Dermatopathology utilizes a novel diagnostic assay to detect genetic mutations to assist in the diagnosis of melanoma and to differentiate benign melanocytic neoplasms from malignant ones. A four probe-fluorescent in situ hybridization assay may improve early classification of melanomas and has been demonstrated to aid diagnosis of cases that are pathologically challenging.

Non-melanoma Skin Cancer Expertise. Stanford Leads the Way in Novel Medical Therapy for Basal Cell Carcinomas (BCC). The Basal Cell Carcinoma Research Group at Stanford is leading several clinical studies to assess novel therapies for non-melanoma skin cancers. Stanford Dermatology clinical-investigators and basic scientists conducted pivotal research in the use of the recently FDA-approved drug, vismodegib, for patients with advanced basal cell carcinoma, including those with inoperable tumors and metastatic disease. This drug stems from basic research on the hedgehog pathway at Stanford over the past 14 years and is the first drug in a new class of anti-tumor agents.

Stanford Dermatology researchers Anthony Oro, MD, PhD (Professor of Dermatology), Anne Chang, MD (Assistant Professor of Dermatology and Director of Clinical Trials), and Jean Tang, MD, PhD (Assistant Professor of Dermatology) have pioneered the study of this agent in patients with locally aggressive and metastatic BCCs, as well as those BCCs that derive from patients with basal cell nevus syndrome (BCNS), a genetic disorder than results in the formation of hundreds of skin cancers. Drs. Oro and Chang contributed to the industry-sponsored pivotal trial that provided the data for FDA approval of vismodegib. An article on this is currently in press in the New England Journal of Medicine. Dr. Tang has also just published an article as lead author in the New England Journal of Medicine detailing the chemopreventive effect of vismodegib in patients with BCNS.

Ongoing research involving this class of drugs, termed hedgehog pathway inhibitors, is in progress at Stanford for locally advanced tumors that are not curable with surgery or in whom surgery...
would lead to loss of vital function or unacceptable morbidity or for metastatic BCC. An additional clinical trial is available for patients with operable BCCs to determine whether the drug decreases the amount of surgery needed. In addition, Stanford BCC specialists are studying mechanisms of drug resistance to improve treatment response to Smoothened inhibitors. Stanford now offers an Advanced Basal Cell Carcinoma Clinic comprised of multidisciplinary cancer specialists for patients with aggressive and/or inoperable BCC.

**Merkel Cell Carcinoma**

Merkel cell carcinoma, also called neuroendocrine cancer of the skin, is a rare skin cancer, although incidence is on the rise in the US. Merkel cell carcinoma (MCC) is usually found on the sun-exposed areas of the head, neck, arms, and legs of older, fair-complexioned individuals but can occur in people of other races and ages. Merkel cell carcinoma grows rapidly and often metastasizes to other parts of the body. Even relatively small tumors are capable of metastasizing. When the disease spreads, it tends to spread to the regional (nearby) lymph nodes and may also spread to the liver, bone, lungs, and brain. For this reason, the Stanford Merkel Cell Program offers a multidisciplinary approach to the treatment of MCC, utilizing the expertise of Stanford surgeons for wide local excision and SLNB staging. Merkel cell carcinoma is very sensitive to radiation therapy, and thus, most patients will benefit from adjuvant radiation to the primary tumor site following resection, as well as to the regional lymph node basin in the event that the SLNB is positive for metastasis. Treatment of Merkel cell carcinoma depends on the stage of the disease, and the patient’s age and overall condition. Under Dr. Krathen’s direction, the Multidisciplinary MCC Program at Stanford is pursuing research regarding newer immunotherapies to treat advanced disease.

**CLINICAL TRIALS INCLUDE:**

**Melanoma:**

- A Phase III Randomized Study of Adjuvant Ipilimumab Anti-CTLA4 Therapy Versus High-Dose Interferon Alfa-2b for Resected High-risk Melanoma Stage III B, III C, or IV (M1a, M1b) (ECOG1609)
- A Phase II Trial of Dasatinib in Patients with Unresectable Locally Advanced or Stage IV Mucosal, Acral and Solar Melanomas (ECOG2607)
- A Pilot Study of Ipilimumab in Subjects with Stage IV Melanoma Receiving Palliative Radiation Therapy (MEL0005)
- A Pilot Study of Vitamin D supplements for reduction of melanoma-associated genes in women (SKIN0010) (Soon to Open)

**Basal Cell Carcinoma:**

- A Phase 2 Randomized Double Blind Study of Efficacy and Safety of Two Dose Levels of LDE225 in Patients with Locally Advanced or Metastatic Basal Cell Carcinoma (SKIN0008)
- Phase II Biomarker Trial to Evaluate the Efficacy of Itraconazole (Oral Antifungal Agent) in Patients with Basal Cell Carcinoma (SKIN0004)
- A pilot open-label study to examine the safety and efficacy of oral LDE225 in patients with locally advanced or metastatic basal cell carcinoma who have been previously treated with non-LDE225 Smoothened inhibitor(s)
- A phase II, multicenter open-label three-cohort trial evaluating the efficacy and safety of vismodegib (GDC0449) in operable basal cell carcinoma (BCC)
The Stanford Sarcoma Program participates in a variety of sarcoma clinical trials, plays an active role in SARC (Sarcoma Alliance for Research through Collaboration), and offers a multidisciplinary, collaborative approach to treatment, diagnostics, and prevention.

**STANFORD SARCOMA CLINICAL TRIALS FOCUS ON:**

- Targeted therapies such as tyrosine kinase inhibitors for gastrointestinal stromal tumors (GIST) and other sarcomas.
- Newer drugs such as denosumab for giant cell tumors and nilotinib for pigmented villonodular sarcomas. In addition, a novel hypoxia-activating agent, TH302, is under intense investigation for high grade soft tissue sarcomas.
- Collaborations with:
  1. Dana Farber Cancer Institute
  2. MD Anderson Sarcoma Center
  3. University of Michigan Cancer Center in cooperative trials through SARC. SARC is an international organization facilitating research partnership among sarcoma researchers, physicians, and medical institutions to establish new models in sarcoma treatment, education, and prevention.

**THE PROGRAM FEATURES:**

1. Surgical, radiation, and medical oncologists
2. Sarcoma focused experts from pathology, interventional and diagnostic radiology, nuclear medicine, and genetics;
3. Nurse coordinators, nurse practitioners, physician assistants, social workers, and dietitians.

Among the experienced specialists are surgeons Jeffrey A. Norton, MD, The Robert L. and Mary Ellenburg Professor in Surgery, and David G. Mohler, MD, Clinical Professor, Orthopaedic...
Surgery; and pathologists Jan Matthijs van de Rijn, MD, PhD, Professor of Pathology, and Robert West, MD, Associate Professor of Pathology, both of whom research gene profiling.

**STANFORD SARCOMA PROGRAM HIGHLIGHTS:**

- **Sarcoma Tumor Board That Meets on a Weekly Basis.**
  New patients, as well as other challenging cases, are presented to this multidisciplinary team. The patient’s radiographs are reviewed by expert radiologists, including the nuclear medicine team. The pathology slides are reviewed in tumor board by pathologists specializing specifically in sarcoma histology. The team of medical oncologists, surgeons, and radiation oncologists then discuss the best treatment course for the patient.

- **Sarcoma Subspecialty Surgeons** who perform innovative surgical techniques in treating the most difficult sarcoma cases with complex surgical problems.

- **Multidisciplinary Sarcoma Clinics** that enable patients to undergo concurrent consultations from multiple disciplines such as a medical oncologist, oncological surgeon, and radiation oncologist, often at the same appointment.

- **Interventional Radiology Service** that offers chemoembolization, radiofrequency ablation, and radioembolization of primary liver sarcomas as well as limited metastases to the liver.

- **Stereotactic Body Radiation Therapy** that provides targeted delivery of radiotherapy for more localized lesions or limited metastatic foci.

- **Intraoperative Radiotherapy** that allows delivery of high dose radiation therapy in the operating room after removal of the tumor mass, leading to better local control.

**CLINICAL TRIALS INCLUDE:**

- **Paclitaxel in Combination with Bevacizumab (Avastin®) for the Treatment of Metastatic or Unresectable Angiosarcoma (SARCOMA0006)**

- **A Phase II Pilot Study of Cyclophosphamide, Doxorubicin, Vincristine Alternating with Irinotecan and Temozolomide in Patients with Newly Diagnosed Metastatic Ewing’s Sarcoma (SARCOMA0007)**

- **A Randomized Controlled Study of YONDELIS (Trabectedin) or Dacarbazine for the Treatment of Advanced Liposarcoma or Leiomyosarcoma Previously Treated with an Anthracycline and Ifosfamide (SARCOMA0008)**

- **A Randomized, Open-label, Multicenter, Phase 3 Study to Compare the Efficacy and Safety of Eribulin with Dacarbazine in Subjects with Soft Tissue Sarcoma (SARCOMA0009)**

- **A Randomized Phase 3, Multicenter, Open-Label Study Comparing TH-302 in Combination with Doxorubicin vs. Doxorubicin Alone in Subjects with Locally Advanced Unresectable or Metastatic Soft Tissue Sarcoma (SARCOMA0010)**

- **A Phase IIb/III Multicenter Study Comparing the Efficacy of Trabectedin Administered as a 3-hour or 24-hour Infusion to Doxorubicin in Patients with Advanced or Metastatic Untreated Soft Tissue Sarcoma (SARCOMA0011) (Soon to Open)**

- **An Open-label, Multi-center, Phase II Study of Denosumab in Subjects with Giant Cell Tumor of Bone (BONE0004)**

- **A Multi-Center Single Agent Phase II Study of the Efficacy of Nilotinib in Patients with Relapsed or Metastatic Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor/Diffuse-Type Giant Cell Tumor (BONE0006)**

- **A Phase II Study of Pazopanib in Patients with Imatinib and Sunitinib Refractory or Intolerant Gastrointestinal Stromal Tumors (GIST0003)**

*highlighted studies are Stanford investigator initiated*