Welcome to the Fall 2013 issue of the Stanford Cancer Institute (SCI) 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. Many of these trials provide access to novel therapies including novel “targeted” agents and immunotherapeutic options not available in the community.

As the co-leader of the Gastrointestinal Oncology Program I am pleased to introduce this issue that showcases our multi-disciplinary programs in Gastrointestinal (GI) Oncology, Skin Cancer, and Sarcoma. Each program offers weekly Tumor Boards that provide an ideal mechanism to present challenging cases and discuss treatment options with all relevant subspecialists. The newsletter also includes a listing of Phase I and II trials from our Developmental Therapeutics Program.

The Gastrointestinal Oncology Program is made up of a multidisciplinary team of specialists who focus on malignancies of the GI tract. This includes both rare (e.g. GI Stromal and neuroendocrine tumors) and common malignancies (gastric, colon, pancreas). Currently we have 15-20 clinical trials that range from multimodality trials (e.g. radiation and chemotherapy for esophageal, pancreas and rectal) to new chemo and targeted regimens for neuroendocrine and gastric cancers to immunotherapeutic trials for gastroesophageal, pancreas and colorectal cancers. While the article will detail the many trials offered, I would like to highlight three trials that demonstrate the breadth of activity in our program: (1) a randomized vaccine study for resected pancreas cancer; (2) a Cyberknife trial with chemotherapy for locally advanced pancreas cancer; and (3) novel targeted agents for gastro-esophageal cancers.

The Skin Cancer Program at the Stanford Cancer Institute is a leading innovator in the prevention and treatment of skin cancer, and offers novel therapies for melanoma, basal cell carcinoma, squamous cell carcinoma, Merkel cell carcinoma, cutaneous lymphoma, and supportive Dermato-Oncology. The Skin Cancer Program has expanded its membership and programs significantly in the past year, and now includes additional surgical offerings. You are encouraged to read the article about this program, which details our achievements, along with the many exciting new research activities and recently added faculty investigator specialists now working in Skin Cancer.

The Sarcoma Program’s clinical trials focus on targeted therapies and newer drugs such as denosumab and nilotinib. In addition, a novel hypoxia-activating agent, TH302, is under intense investigation for high grade soft tissue sarcomas. The program includes sarcoma specialty surgeons, 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, MD Anderson Sarcoma Center, and the University of Michigan.

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. 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
Professor of Medicine
Stanford Cancer Institute
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.

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

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.

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. SCI also has the first Trilogy and TrueBeam systems for clinical use in the Western US. 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’s 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.

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 therapies 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 oncologist.
- Multicenter trial led by Stanford with Memorial Sloan Kettering and Johns Hopkins that is investigating the role of stereotactic radiation surgery for unresectable pancreas cancer. Again, the standard “chemo” can be administered by the patient’s local oncologist.
- Phase I/II trials using novel molecularly targeted agents for metastatic colorectal and gastro-esophageal cancers. Molecularly targeted therapies include drugs which specifically bind to key molecules on or in the tumor cells and immunotherapeutic antibodies that are capable of triggering an immune response against the cancer. These promising strategies are in their infancy in development yet are already showing encouraging clinical results in patients.
- 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

Colorectal Adenocarcinoma

Metastatic 2nd Line
- A Phase 2 Randomized, Double-Blinded, Placebo-Controlled Study to Evaluate the Efficacy and Safety of GS-0624 Combined with FOLFIrI as Second Line Treatment for Metastatic KRAS Mutant Colorectal Adenocarcinoma that Has Progressed Following a First Line Oxaliplatin- and Fluoropyrimidine-Containing Regimen (COR0010)
- 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 (Colorectal Cancer) and Relapsed Refractory B-cell Non-Hodgkin’s Lymphoma (B-NHL) (VAR0071)

A Pilot Phase III Study to Evaluate Overall Survival using MIAP1 as a Monotherapy in Metastatic Colorectal Cancer Patients with Cachexia (COR0071)
STANFORD SARCOMA PROGRAM HIGHLIGHTS

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 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.
**Stanford Sarcoma Program continued**

- 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 foot.
- 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**

- **SOON TO OPEN: A Phase 2 Study of Linsitinib (OSI-906) in Pediatric and Adult Wild Type Gastrointestinal Stromal Tumors (SARC-022)**
- **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 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 Multi-Center Single Agent Phase II Study of the Efficacy of Nilotinib in Patients with Relapsed or Metastatic Pigmented Vitilomacular Synovitis/Tenosynovial Giant Cell Tumor/Diffuse-Type Giant Cell Tumor (BONE0006)**
- **A Feasibility Study to Evaluate the Safety and Initial Effectiveness of ExAblate MR Guided Focused Ultrasound Surgery in the Treatment of Pain Resulting from Metastatic Bone Tumors with the ExAblate 2100 Conformal Bone System (BONE0007)**

**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.

**ONLINE CME COURSE**

**Practical tips to improve Asian American participation in cancer clinical trials**

Presented by the Stanford Cancer Institute at Stanford University School of Medicine

The Continuing Medical Education course, Practical tips to improve Asian American participation in cancer clinical trials, is designed to meet the educational needs of a national audience of physicians and allied health professionals who specialize in family practice, primary care, internal medicine and oncology.

Duration & Format: 1-hour, internet-based

CME Processing Fee: $20; fee waived for the first 200 learners who complete all CME activities required for this course.

Internet Enduring Material Sponsored by the Stanford University School of Medicine

For more information about the course and CME credit, please visit: coursera.org/course/clinicaltrials

**The Skin Cancer Program**

Providing: Innovative Prevention and Treatment and Novel Therapy for Melanoma, Basal Cell Carcinoma, High-Risk Squamous Cell Carcinoma, Merkel Cell Carcinoma, and Supportive Dermato-Oncology

**MELANOMA CLINICAL-EPIDEMIOLOGICAL RESEARCH AND PROGRAM DEVELOPMENT**

In January 2013, Robert Haile, DrPH, joined the faculty at Stanford as Professor in the Department of Medicine and Associate Director of Population Sciences at the Stanford Cancer Institute. Major initiatives started by Dr. Haile include enhancing the clinical translational impact of genomics-based research, enhancing biological and behavioral research that will result in earlier detection of cancer, expanding survivorship research, and expanding research in multiple racial/ethnic groups, all of which align with the goals of the Stanford Skin Cancer Program.

The Stanford Pigmented Lesion and Melanoma Program (PLMP) is directed by Susan Swetter, MD, Professor of Dermatology and Physician Leader of the Stanford Cancer Care Program in Cutaneous Oncology, and has spearheaded research designed to prevent melanoma, including chemoprevention studies and early detection strategies to enhance the likelihood of cure. Stanford PLMP members recently collaborated with epidemiologists at the Cancer Prevention Institute of California (CPIc) to assess the survival differences between adolescent and young adult men and women with cutaneous melanoma (published in JAMA Dermatology). Dr. Swetter and CPIc epidemiologists, Christina Clarke-Dur, PhD, MPH and Theresa Keegan, PhD, MS, found that young men were 55% more likely to die of melanoma than age-matched women, despite adjusting for factors that may affect prognoses, such as tumor thickness, histology and location of the
melanoma, as well as the presence and extent of metastasis. These novel findings present further evidence that a biologic mechanism may contribute to the sex disparity in melanoma survival, since adolescent and young adults see physicians less frequently and are less likely to have sex-related behavior differences in skin cancer screening practices compared with older individuals. Dr. Swetter and her research colleagues are exploring potential biologic reasons for the survival difference.

Additional large scale epidemiologic research lead by Jean Tang, MD, PhD, Assistant Professor of Dermatology, Marcia Stefanick, PhD, Professor of Medicine at the Stanford Prevention Research Center, and Dr. Swetter utilized the Women’s Health Initiative Observational Study data and demonstrated that postmenopausal women ages 50 to 79 years who used aspirin had a 21% lower risk of developing melanoma. The risk was even lower (30%) for women who used aspirin for at least 5 years. While this study is not a randomized clinical trial, the observed association is significant and warrants further investigation. Stanford investigators recently initiated the first trial of high dose vitamin D (4,000 IU) on precursor melanoma cells in women.

Further prevention efforts have been directed to Stanford’s outdoor student-athletes and the entire Stanford community through a novel program entitled SUNSPORT™, which stands for Stanford University Network for Sun Protection, Outreach, Research, and Teamwork. This unique initiative stems from collaboration among Stanford Dermatology, Stanford Athletics (including Sports Medicine and Athletic Trainers), Stanford Cancer Institute, Stanford Hospital & Clinics to create an integrated research, education and intervention program dedicated to providing skin cancer risk awareness and sun-protection education to student athletes, fans and supporters, and the Stanford community at large. Research by former Stanford Dermatology resident Dr. Ashley Wysong and Dr. Tang showed the Stanford community at large. Research by former Stanford Dermatology resident Dr. Ashley Wysong and Dr. Tang showed that NCAA athletes spend at least 2 hours per day training or competing outdoors for 8 months of the year or more, with high rates of sunburn reported. As a result, outdoor college athletes are likely at higher risk for skin cancer and melanoma, and SUNSPORT provides skin screening for incoming freshman athletes and works with coaches and trainers to provide direct education to athletes to promote sun protection practices. Plans to expand the educational messages to younger, school-age athletes and outdoor enthusiasts are in progress.

Improved survival in patients with advanced melanoma has remained an elusive goal for the past several decades, with promising and effective immunotherapy and targeted therapies only recently becoming available. Two new drugs were approved for the treatment of advanced disease in 2011, ipilimumab and vemurafenib, and two additional targeted therapy agents were FDA-approved May 2013. Under the direction of medical oncologist, Dr. Sunil Reddy, Clinical Assistant Professor in Medicine, the Stanford PUMP has opened a trial of a vascular revascularization versus placebo in patients with surgically removed high risk cutaneous melanoma (stage IIC and resected stage III lymph node) melanoma. A randomized adjuvant therapy trial assessing the use of both low- and high-dose ipilimumab versus high-dose interferon is in progress for patients with surgically resected stage IIB, IIC, IVa/b melanoma, and a recently opened trial will assess the use of the combination of BRAF and MEK inhibitors in patients with advanced disease. In addition, there will soon be a trial of a MEK inhibitor in patients with metastatic melanoma who harbor the NRAS mutation, which is usually present in the absence of the BRAF mutation, offering a targeted therapy option for BRAF wild-type melanoma.

An estimated one million Americans are currently living with a melanoma diagnosis. As melanoma becomes a more treatable disease in patients with advanced stages, attention to survivorship issues is critical. Stanford melanoma surgeon Ralph Greco, MD, Professor of Surgery, Dr. Swetter, and Kelly Bugos, MS, NP, Manager of the Stanford Cancer Survivorship Program, conducted a needs assessment survey to determine the unmet needs of melanoma survivors previously treated at the Stanford Cancer Center (SCC). Survey results were presented at the annual American Society of Clinical Oncology (ASCO) meeting in May 2013. Both short- and long-term melanoma survivors reported continuing psychosocial symptoms years after treatment, especially anxiety, and expressed a need for education regarding long-term melanoma effects, family risk, protection from future sun damage, and prevention of additional skin cancer. Given these preliminary results, the Stanford PUMP will be establishing a formal Melanoma Survivorship Clinic, along with conducting more research to improve the quality of life for melanoma survivors.

**NEW PROGRAM DEVELOPMENT IN SUPPORTIVE DERMATO-Oncology AND CUTANEOUS MALIGNANCIES DERMATOLOGY AND SURGICAL PROGRAMS**

In the fall of 2012, Dr. Bernice Kwong, Clinical Assistant Professor in Dermatology, initiated the first Supportive Dermato-Oncology Program within the Stanford Cancer Center (SCC). The program offers a kind program allows for direct dermatology evaluation of patients undergoing cancer therapy to address cutaneous complications related to cancer diagnosis and skin side effects of cancer treatment that may severely impact a patient’s day-to-day activities and/or prevent ongoing therapeutic intervention. A large part of Dr. Kwong’s practice involves addressing skin manifestations of graft versus host disease in patients who have undergone bone marrow transplantation. The reception of Dr. Kwong’s efforts in the SCC by both patients and staff has been remarkable, and treating debilitating skin conditions in cancer patients has allowed them to continue treatment in many cases. In 2012, Dr. Michael Krathen, Clinical Assistant Professor of Dermatology, introduced a novel Post-Transplant / High Risk Skin Cancer Clinic in Stanford Dermatology, focused 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. Leadership of this clinic will transition to Clinical Instructor in Dermatology Carolyn Lee, MD, PhD, in the fall of 2013 and will involve ongoing collaboration with medical and surgical oncology colleagues for treatment and prevention approaches.

The PUMP is fortunate to have two Stanford surgeons specializing in head and neck surgical oncology, John Sunwoo, MD and Vasu Divi, MD. 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 laboratory 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. Sunwoo is also working with Lei Xing, PhD, the Director of the Physics Division of Radiation Oncology, and Andrew Quon, MD, co-Director of Nuclear Medicine, to develop novel uses of photothermal imaging to aid the detection of melanoma metastases to lymph nodes, and with Craig Levin, PhD, Professor of Radiology, Physics and Electrical Engineering, to evaluate a gamma camera in the use of sentinel lymph node biopsies. He also manages a clinical database of head and neck sentinel lymph node biopsy cases that will be used to improve our understanding of this approach in the broad context of melanoma surgical management. Dr. Divi, Assistant Professor of Otolaryngology – Head and Neck Surgery, also has a strong clinical interest in the surgical management of head and neck cutaneous malignancies, including melanoma, Merkel cell carcinoma, and high-risk squamous cell carcinoma. His research interests include clinical outcomes for high-risk cutaneous head and neck squamous cell carcinoma and examining tumor biomarkers associated with high-risk disease.

**Collaborative Cutaneous Oncology Surgical Team Expands 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 PUMP features a collaborative team of dermatologic and melanoma surgeons who perform wide local excision, sentinel lymph node biopsy (SLNB) for melanoma staging, as well as resection of more advanced disease. Stanford Clinical Associate Professor Sumaira Asai, MD, Director of Moths and Dermatologic Surgery at the Stanford Medicine Outpatient Center, continues to expand cutaneous surgical treatment of melanoma and nonmelanoma skin cancers in the Dermatology Department. 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. Dr Greco is currently evaluating the role of Spy imaging in identifying sentinel lymph nodes in melanoma patients. 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 TRANSLATIONAL RESEARCH HIGHLIGHTS**

Studies of the innate immune response to melanoma cancer stem cells and what regulates this response are being conducted in the laboratory of Dr. John Sunwoo. He works closely with tumor immunologist Holbrook Kohrt, MD, PhD, Assistant Professor of Medicine, Hematology and Oncology, who is the
Carcinomas

New Immunotherapy Trials

The first potentially curative immunotherapy, ipilimumab, has become a standard of care for patients with advanced melanoma. Over the prior year, a novel immunotherapy agent has been tested in clinical trials with early response rates appearing even more promising. The new immunotherapy, targeting PD-1, stimulates the immune response against the cancer and will be tested at Stanford as a treatment for Mycosis Fungoides (a skin lymphoma) and Merkel Cell Carcinoma under the direction of Dr. Kohrt. He and the Stanford Immunotherapy Team are also examining the combination of ipilimumab and radiation as well as the combination with the new immunotherapy targeting PD-1 for patients with melanoma.

New trial: A Phase II trial of Dasatinib in Patients with Unresectable Locally Advanced or Stage IV Mucosal, Acral and Solar Malignomas (ECOGE2607)

Stanford Professor of Radiation Oncology Susan Knox, MD, PhD, continues to lead a novel trial of the systemic immunotherapy agent ipilimumab, in conjunction with palliative radiation therapy for patients with metastatic melanoma. This study tests whether ipilimumab combined with radiation therapy enhances the body’s ability to attack melanoma—even outside of the radiation field and has been expanded into a phase III trial at Stanford and other collaborating institutions, which will open in the near future.

NON-MELANOMA SKIN CANCER EXPERTISE

Stanford Leadership in Novel Medical Therapy for Basal Cell Carcinomas

The Basal Cell Carcinoma Research Group at Stanford is conducting several clinical studies to assess novel therapies for non-melanoma skin cancers, including basal cell carcinoma.

The Hedgehog Pathway, Target of Multiple Drugs in Skin Cancer

A number of studies have been conducted to inhibit the hedgehog pathway, which plays a critical role in skin cancer. 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. Stanford BCC investigators are nearing completion of a phase 2 clinical trial of a separate hedgehog inhibitor drug, erismodigib. In addition, they are looking for novel treatment regimens that might prolong the tumor responses to hedgehog inhibitor drugs and are studying mechanisms of drug resistance to improve treatment response to smoothened inhibitors.

Stanford Dermatology and Cancer Institute offers an Advanced Basal Cell Carcinoma Clinic comprised of multidisciplinary cancer specialists for patients with aggressive and/or inoperable BCC. Dr. Kavita Saini, MD, PhD, Clinical Assistant Professor of Dermatology, has joined the Basal Cell Carcinoma Group and is collaborating in efforts looking at germline and somatic genetic variants that influence basal cell carcinoma risk, prognosis, and response to therapy.

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. When the disease spreads, it tends to spread to the regional (nearby) lymph nodes and may also spread to the liver, bone, lung, and brain. 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 the direction of Dr. Kohrt, the Multidisciplinary MCC Program at Stanford is pursuing research regarding newer immunotherapies to treat advanced disease.

CLINICAL TRIALS INCLUDE Melanoma

• A Phase II Randomized Study of Adjuvant Ipilimumab Anti-CTLA4 Therapy Versus High-Dose Interferon Alfa-2b for Resected High-risk Melanoma Stage IIIB, IIC, or IV (M1a, M1b) (ECOGE1609)

• A Phase II Trial of Dasatinib in Patients with Unresectable Locally Advanced or Stage IV Mucosal, Acral and Solar Malignomas (ECOGE2607)

• A Pilot Study of Ipilimumab in Subjects with Stage IV Melanoma Receiving Palliative Radiation Therapy (MEL0005)

• A Phase III, Randomized, Double-blind, Placebo-controlled Study of Vemurafenib (ROS1852462) Adjuvant Therapy in Patients with Surgically Resected, Cutaneous BRAF-Mutant Melanoma at High Risk for Recurrence (MEL0006)

• A Phase III, Double-blind, Placebo-Controlled Study of Vemurafenib Versus Vemurafenib plus GDC-0973 in Previously Untreated BRAF-V600-Mutation Positive Patients with Unresectable Locally Advanced or Metastatic Melanoma (MEL0007)

• The NEMO Trial (NRAS Melanoma and MEK Inhibitor): A Randomized Phase III, Open Label, Multicenter, Two-Arm Study Comparing the Efficacy of MEK162 Versus Dacarbazine in Patients with Advanced Unresectable or Metastatic NRAS Mutation-Positive Melanoma (MEL0008)

• A Phase III Study of Intratumoral Injection of Ipilimumab in Combination with Local Radiation in Melanoma, Non-Hodgkin Lymphoma and Colorectal Carcinoma (VAR0006)

• Pilot Trial to Evaluate the Effect of Vitamin D on Melanocyte Biomarkers in Women (SKIN0101)

• Testing the Efficacy of Indocyanine Green Imaging (ICG-SPR) in the Identification of Sentinel Lymph Nodes in Patients with Malignant Melanoma (MEL010)

Basal Cell Carcinoma

• 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 Inhibitors (SKIN0009)

• A Pilot Study to Investigate the Off Label Use ofArsenic Trioxide for Basal Cell Carcinoma (BCC) (SKIN0215)

• A Phase II Study of Capcetabine in Patients with Advanced or Recurrent Squamous Cell Carcinoma of the Skin (SKIN0316)

• A Randomized, Double-Blinded, Regimen-Controlled, Phase II, Multicenter Study to Assess the Efficacy and Safety of Two Different Vismodegib Regimens in Patients with Multiple Basal Cell Carcinomas (SKIN0117)
Stanford Cancer Center’s Developmental Therapeutics Program, 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), Dimitri Colevas (head and neck cancers), George Fisher and Pamela Kunz (GI cancers), Mark Pegram and Melinda Telli (breast 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.

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

**PHASE 1 STUDIES**

**Multiple Solid Tumor Sites**

- A Phase I, Open-Label, Dose-Escalation Study of the Safety and Pharmacokinetics of MPDL3280A Administered Intravenously as a Single Agent to Patients with Locally Advanced or Metastatic Solid Tumors (VAR0082)
- A Phase 1, Open-label, Dose-escalation, Safety and Pharmacokinetic Study of CDX-1127 in Patients with Selected Refractory or Relapsed Hematologic Malignancies or Solid Tumors (VAR0081)

**Lymphomas**

- 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 Lymphoma (NHL) (LYMNHL0092)

**PHASE 2 STUDIES**

**Thymic Cancers**

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

**Small Cell Lung Cancer and Other High-Grade Neuroendocrine Tumors**

- A Phase Ia Intrapatient Dose Escalation Study of Desipramine in Small Cell Lung Cancer and Other High-Grade Neuroendocrine Tumors (VAR0087)

**Squamous Cell: Head & Neck, Non-small Cell Lung, Skin, Cervical, Penile, Anal, and Esophageal Cancers**

- A Phase II Study of Oral Rigosertib in Patients with Relapsed or Metastatic, Platinum-resistant, Human Papillomavirus Positive or Negative Squamous Cell Carcinoma (VAR0092)

- 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)

- A Phase I/II Study of Intratumoral Injection of Iplimumab in Combination with Local Radiation in Melanoma, Non-Hodgkin Lymphoma and Colorectal Carcinoma (VAR0090)

*highlighted studies are Stanford investigator initiated*