Welcome to the second 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 available at the NCI-designated Stanford Cancer Center. Along with our own physician-led studies, which are unique to Stanford, we offer NCI Cooperative Group and industry sponsored trials. One of our more than 300 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 presents the clinical trials and novel treatments offered in our multi-disciplinary programs in Gastrointestinal (GI) Oncology, Cutaneous Oncology, and Sarcoma, as well as early-phase clinical trials from our Developmental Therapeutics Program. Each program holds weekly Tumor Board Meetings that provide an ideal mechanism to present challenging cases and discuss treatment options with all relevant subspecialists.

The Gastrointestinal Oncology Program conducts studies on a wide variety of promising new agents. The physician members of this program reflect the multi-disciplinary care available to your patients. Featured trials include a randomized vaccine study of resected pancreas cancer, and for patients with unresectable pancreas cancer, Stanford is currently leading a multicenter trial with Memorial Sloan Kettering and Johns Hopkins investigating the role of stereotactic radiosurgery (CyberKnife®).

The Cutaneous Oncology Program is developing better ways to prevent and treat melanoma and basal cell carcinoma. The article on this program highlights the translational research activities of our physicians along with the available clinical trials.

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 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.

Douglas W. Blayney, MD
Ann & John Doerr Medical Director, Stanford Cancer Center
Professor of Medicine & Medical Oncology

RESOURCES:
Clinical Trials Recruitment Specialist
650.498.7061
Referral Center
1.866.742.4811
Clinical Trials Web-based Search Engine
cancer.stanford.edu/trials
Stanford Gastrointestinal Oncology Program
Integrating the Latest Laboratory Discoveries, Technological Innovations, and Support Services into Cancer Patient Care

Stanford’s Gastrointestinal (GI) Oncology Program integrates the latest laboratory discoveries, technological innovations, and support services into the care of its cancer patients. As an academic cancer center, Stanford Cancer Center (SCC) offers cutting edge molecular and imaging capabilities to better define each cancer. The SCC team of specialists then develops a treatment strategy personalized to the patient’s needs. The SCC also offers, when appropriate, novel therapeutic agents through a variety of clinical trials.

GI ONCOLOGY MULTIDISCIPLINARY TEAM OF SPECIALISTS
The GI Oncology multidisciplinary team consists of specialists who focus on cancers of the GI tract. This includes 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, 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 Surgeries: Specialists in surgical oncology can sometimes remove cancers using a laproscope, 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.

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.

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.
• Multi-center trial led by Stanford with Memorial Sloan Kettering and Johns Hopkins that is investigating the role of stereotactic radiosurgery (CyberKnife) 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 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 TRIALS INCLUDE:
• Anal Carcinoma:
  • Phase II Trial of Cetuximab Plus Capecitabine, 5-Fluorouracil and Radiation in Immunocompetent Patients with Anal Carcinoma (ECOG3200)
• Cholangiocarcinoma:
  • A Phase II Trial of Adjuvant Capecitabine/Gemcitabine Chemotherapy Followed by Concurrent Capecitabine and Radiotherapy in Extrabiliary Cholangiocarcinoma (EHC)(SWOGS0809)
  • Phase II Study of Stereotactic Body Radiotherapy (SBRT) and Chemotherapy for Unresectable Cholangiocarcinoma Followed by Liver Transplantation (HEP0032)
• Colon & Rectum Cancer:
  • FOR PATIENTS WITH KRAS WILD TYPE, IRINOTECAN REFRACTORY DISEASE WHO HAVE NOT YET HAD AN EGFR INHIBITOR: A Phase 2 Study of EZN-2206 (PEG-SN38) Administered with or without Cetuximab in Patients with Metastatic Colorectal Carcinoma (mCRC) (CO10009)
  • Statin Polyp Prevention Trial in Patients with Resected Colon Cancer (NASIBP5)
• Gastroesophageal Adenocarcinoma:
  • FIRST LINE METASTATIC DISEASE: A Phase II Study of Capecitabine, Carprofenib, and Bevacizumab for Metastatic or Unresectable Gastroesophageal Junction and Gastric Adenocarcinoma (GX01002)
  • SECOND LINE METASTATIC DISEASE: Randomized Phase II Study of Paclitaxel with or without the Anti-IGF-IR mAb

• Highlighted studies are Stanford Investigator Initiated
The Stanford Sarcoma Program offers a multidisciplinary, collaborative approach to treatment, diagnostics and prevention, participates in a variety of sarcoma clinical trials, and plays an active role in SARC (Sarcoma Alliance for Research through Collaboration).
The Stanford Pigmented Lesion and Melanoma Program (PLMP) is a diagnostic surgical procedure used to determine whether microscopic melanoma cells have spread to the regional lymph nodes. Stanford surgeons are now investigating new technologies to improve SLN detection. The Stanford surgical team includes Ralph Greco, MD, Professor of Surgery; Mike Yao, MD, Associate Professor of Head and Neck Surgery; Jeffrey Norton, MD, Chief of Surgical Oncology and General Surgery; and Subhro Sen, MD, Clinical Assistant Professor of Plastic and Reconstructive Surgery. This program expansion complements Hayes Gladstone, MD, Associate Professor of Dermatology, who regularly performs cutaneous melanoma surgery at Stanford. In addition, Laura Morris, RN, BSN, recently joined as nurse coordinator to provide a vital link between patients and melanoma health care providers.

MELANOMA CLINICAL-EPIDEMIOLOGICAL RESEARCH: Chemoprevention Trials for Patients at Increased Risk of Melanoma. As Stanford Principal Investigator for the National Cancer Institute/University of Arizona Phase I/II Cancer Chemoprevention Consortium, Dr. Swetter recently completed patient accrual for one of the first national chemoprevention trials for melanoma, a strategy designed to prevent the development of cancer in high-risk individuals. The trial involved the use of a nonsteroidal anti-inflammatory agent (similar to ibuprofen) in patients with atypical moles.

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.

MELANOMA TRANSLATIONAL RESEARCH HIGHLIGHTS: Interferon Signaling Defects in the Immune System of Melanoma Patients. The work of Peter Lee, MD, Associate Professor of Medicine (Hematology), found that interferon signaling defects in the immune system 1) are common in patients with melanoma and other cancers (breast and gastrointestinal) and 2) likely represent a common cancer-associated mechanism of immune dysfunction, which prevents cancer eradication in the host. Dr. Lee’s continued research in this area could lead to new and more effective treatments for patients.

Stem Cell Research. Stanford melanoma team members collaborate in the area of stem cell research with Irving Weissman, MD, Director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine. Dr. Weissman and colleagues have proposed that 1) a self-renewing population of cancer stem cells can lead to cancer dissemination and establishment of distant metastases; and 2) that these cells may be targets for more successful therapies in the cancer patient. In human melanoma, Dr. Weissman’s group found that stem cells express a certain neural crest nerve growth factor receptor against which immunotherapies and clinical trials might eventually be tested. Identification of genetic alterations and pathways of melanoma development will provide powerful therapeutic options for patients diagnosed with all stages of melanoma.

KIT Proto-oncogene Inhibition May Treat Certain Melanoma Subtypes. Targeted therapy against specific mutations in melanoma has gained recent attention as one of the most successful means of achieving responses in advanced disease over the past 30 years. KIT is a proto-oncogene, meaning that over-expression or mutations of this protein can lead to cancer. Research thus far supports the hypothesis that inhibiting KIT may be therapeutic in patients with acral, mucosal, or cutaneous melanoma with evidence of chronic sun damage. Under the guidance of Sunil Reddy, MD, Clinical Instructor in Medicine (Oncology), Daniel Chen, MD, PhD, Adjunct Clinical Instructor in Medicine (Oncology), and Joseph Mollick, MD, PhD, Clinical Instructor in Medicine (Oncology), Stanford is participating in a national clinical trial assessing the use of a KIT inhibitor in patients with advanced acral, mucosal, and sun-induced melanomas.

Iplimumab Offered to Metastatic Melanoma Patients. A novel and very promising immunotherapy agent, ipilimumab, is an antibody used to activate the immune system. This antibody, directed against T cells, removes one of their regulatory mechanisms, effectively “turning off the brakes” and creating an immune response to the tumor. Under an expanded access program, ipilimumab is currently available to patients with advanced melanoma, and recent FDA approval of this agent will increase its use in clinical practice. In upcoming trials, this drug will be used for patients with a history of surgically resected melanoma that is at high risk of recurrence.

Stanford Leads the Way in Novel Medical Therapy for Basal Cell Carcinomas (BCC). Clinical and basic science investigators within the Stanford Department of Dermatology are advancing the treatment of the most common cancer, basal cell carcinoma, which accounts for over 3 million cases annually in the US. Hedgehog Pathway Inhibitors for BCC Patients. The Basal Cell Carcinoma Research Group at Stanford is testing a new class of agent, hedgehog pathway inhibitors (HPI) in BCC patients. With its move to the new Stanford Medicine Outpatient Center in Redwood City, which has tripled the size of its clinic, the new facility provides the space needed to test new therapies for skin cancer. Stanford is currently one of the largest US centers testing this new class of inhibitors for patients with BCC.

Phase 1 and 2 Studies of Smoothened Inhibitors for Locally Advanced and Metastatic Basal Cell Carcinomas. Anne Chang, MD, and Anthony Oro, MD, PhD, are currently treating patients in Phase I and Phase II clinical trials using a class of oral HPIs called smoothened inhibitors for completely advanced and metastatic basal cell carcinomas. These patients have few viable options, and preliminary results have been very promising. Additional studies include following a larger cohort of patients with advanced disease to test drug effectiveness and resistance.

Smoothed Inhibitors in Gorlin Syndrome Patients. Studies are underway to investigate the effectiveness of smoothed inhibitors to shrink tumors in less advanced, but much more common basal cell cancers. Jean Tang, MD, PhD, is part of an investigator initiated, double-blind trial to test smoothed inhibitors in patients with Gorlin Syndrome.

Trarcanozole as an HPI for Shrinking BCC Tumors. Dr. Tang is a key investigator in a research group demonstrating that the common anti-fungal drug, trarcanozole, has activity as an HPI. Her study demonstrated in a mouse model of BCC that this oral drug can significantly shrink BCC tumors. Dr. Tang is now enrolling patients with advanced BCCs, who would ordinarily receive MOHS surgery, in a study to test the effectiveness of trarcanozole.

The Stanford Pigmented Lesion and Melanoma Program (PLMP) is developing better ways to prevent melanoma, treat the disease with less harm, and improve understanding of factors that affect patients’ health and wellness. The Stanford PLMP is directed by Susan M. Swetter, MD, Professor of Dermatology, University of Southern California. Dr. Peng has collaborated of the Pigmented Lesion Clinic at the Norris Cancer Center, Dermatology Faculty and Melanoma Team in 2010. Former Director directed by Susan M. Swetter, MD, Professor of Dermatology, that affect patients’ health and wellness. The Stanford PLMP is developing better ways to prevent melanoma, treat the disease with less harm, and improve understanding of factors that affect patients’ health and wellness. The Stanford PLMP is directed by Susan M. Swetter, MD, Professor of Dermatology, University of Southern California. Dr. Peng has collaborated of the Pigmented Lesion Clinic at the Norris Cancer Center, Dermatology Faculty and Melanoma Team in 2010. Former Director directed by Susan M. Swetter, MD, Professor of Dermatology, University of Southern California. Dr. Peng has collaborated of the Pigmented Lesion Clinic at the Norris Cancer Center, Dermatology Faculty and Melanoma Team in 2010. Former Director
CLINICAL TRIALS INCLUDE:

**Basal Cell and Squamous Cell Carcinomas:**
- An Open-label, Multicenter Extension Study of GDC-0449 (Hedgehog Pathway Inhibitor) in Patients Treated with GDC-0449 in a Previous Genentech-Sponsored Phase I or Phase II Cancer Study (SKIN0003)
- Pilot Biomarker Trial to Evaluate the Efficacy of Itraconazole in Patients with Basal Cell Carcinomas (SKIN0004)
- A Phase I Study of IPI-926 in Patients with Advanced and/or Metastatic Solid Tumor Malignancies (SKIN0005)
- A Phase II, Multicenter, Open-label, Two-cohort Trial Evaluating the Efficacy and Safety of GDC-0449 in Operable Basal Cell Carcinoma (BCC) (SKIN0006)
- A Single Arm, Open-Label, Expanded Access Study of GDC-0449 in Patients with Locally Advanced or Metastatic Basal Cell Carcinoma (SKIN0007)

**Skin Cancer**
- A Multicenter Treatment Protocol for Expanded Access Use of Iplimumab (BMS-734016) Monotherapy in Subjects with Unresectable Stage III or Stage IV Melanoma (MEL0003)
- E2607, A Phase II Trial of Dasatinib in Patients with Unresectable Locally Advanced or Stage IV Mucosal, Acral and Solar Melanomas (ECOGE2607)
- E1608 - A Phase II Trial of GM-CSF Protein plus Ipiilimumab in Patients with Advanced Melanoma (ECOGE1608)
- E1609, A Phase III Randomized Study of Adjuvant Iplimumab Anti CTLA4 Therapy Versus High-Dose Interferon Alfa-2b in Patients with Resected High-Risk Stage III B, IIIC, or IV Melanoma (not yet active) (ECOGE1609)

**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)

**Melanoma:**
- A Multicenter Treatment Protocol for Expanded Access Use of Iplimumab (BMS-734016) Monotherapy in Subjects with Unresectable Stage III or Stage IV Melanoma (MEL0003)
- E2607, A Phase II Trial of Dasatinib in Patients with Unresectable Locally Advanced or Stage IV Mucosal, Acral and Solar Melanomas (ECOGE2607)
- E1608 - A Phase II Trial of GM-CSF Protein plus Ipiilimumab in Patients with Advanced Melanoma (ECOGE1608)
- E1609, A Phase III Randomized Study of Adjuvant Iplimumab Anti CTLA4 Therapy Versus High-Dose Interferon Alfa-2b in Patients with Resected High-Risk Stage III B, IIIC, or IV Melanoma (not yet active) (ECOGE1609)

**hightlighted studies are Stanford investigator initiated**