Clinical Research

Newsletter for Colleagues in the Community

Stanford Cancer Institute
A National Cancer Institute Designated Cancer Center
Stanford MEDICINE

Welcome to the Spring 2016 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 Physician Leader of the Gastrointestinal Oncology (GI) Program and Director of the Neuroendocrine Tumor Program, I am pleased to introduce this issue that showcases our multi-disciplinary programs in GI, Cutaneous 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 Gastrointestinal Oncology Program is comprised of a multidisciplinary team of specialists who focus on malignancies of the GI tract, including both rare (e.g. GI stromal and neuro-endocrine tumors) and common cancers (gastric, colon, and pancreas). Stanford is a high volume referral center for neuroendocrine tumors (NETs) and will formally launch a NET Program in Spring 2016. This program will bring together clinical and research expertise in areas such as medical oncology, surgical oncology, interventional radiology, nuclear medicine, endocrinology, and survivorship. The GI Program currently offers nearly 25 clinical trials that range from multimodality trials to new chemo- and molecularly-targeted therapies, including drugs that specifically bind to key molecules on or in the tumor cells, and immunotherapeutic antibodies capable of triggering an immune response against the cancer.

The Skin Cancer Program at the Stanford Cancer Institute is a leading innovator in the research and treatment of all types of skin cancer, including melanoma and atypical melanocytic neoplasms (both adult and pediatric), high-risk and solid organ transplant-associated squamous cell carcinoma, advanced basal cell carcinoma, Merkel cell carcinoma, and rarer cutaneous adnexal malignancies. It encompasses several distinct clinical programs and is led by Dr. Susan Swetter, Professor of Dermatology/Cutaneous Oncology. Clinics are held in the Stanford Cancer Center in Palo Alto and the recently-opened Cancer Center South Bay (CCSB) facility in San Jose.

The Sarcoma Program's clinical trials focus includes tyrosine kinase inhibitors for gastrointestinal stromal tumors (GIST) and other sarcomas. The program offers access to newer drugs such as aldoxorubicin and regorafenib. In addition, a novel hypoxia-activating agent, TH302, is under intense investigation for high-grade soft tissue sarcomas. The program features specialists in sarcoma surgery, interventional radiology, stereotactic body radiation therapy, and intraoperative radiotherapy. We are an active participant in clinical trials conducted in collaboration with Dana Farber Cancer Institute, MD Anderson Sarcoma Center, and the University of Michigan Cancer Center through SARC (Sarcoma Alliance for Research through Collaboration).

Phase 1 and 2 trials from our Developmental Therapeutics Program are also included in the newsletter. This program, led by Dr. Shivaani Kummar, former leader of the National Cancer Institute's Developmental Therapeutics Clinic and Early Clinical Trials Development Program, is continually expanding its trial offerings.

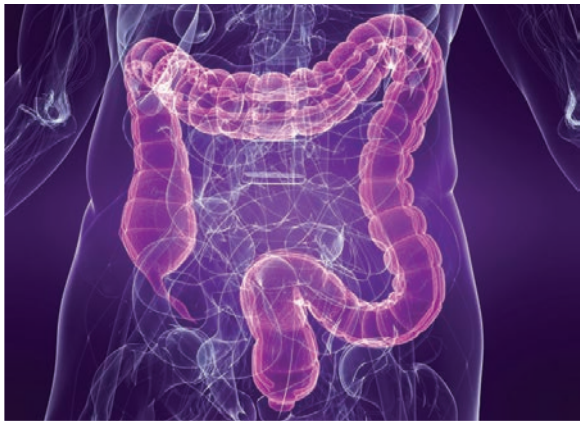
We hope that you will consider a Stanford Cancer Institute clinical trial when you deem it appropriate to refer a patient to an academic medical facility.

Pamela L. Kunz, MD

Assistant Professor of Medicine/Oncology
Director, Stanford Neuroendocrine Tumor Program and Physician Leader, Gastrointestinal Clinical Research Program

Stanford Gastrointestinal Oncology Pro

Translating Discovery to Innovative Care



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.

FEATURES OF THE PROGRAM INCLUDE

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 therapeutics that target the molecular features of an individual's tumor and develop immunotherapies that harness the power of a patient's immune system.

Trials of Particular Interest

- 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 I/II trials using novel molecularly targeted agents for metastatic colorectal and gastro-esophageal cancers. Molecularly targeted therapies include drugs that specifically

bind to key molecules on or in the tumor cells and immuno-therapeutic antibodies that are capable of triggering an immune response against the cancer. These promising strategies are showing encouraging clinical results in patients with GI cancers.

- In collaboration with Johns Hopkins, a trial for second line metastatic pancreas cancer patients using a dual vaccine strategy with or without the PD1 antibody, nivolumab. The same collaboration has led to the identification of MSI tumors having exquisite sensitivity to PD-1 directed therapies and this trial continues to accrue all tumor histologies that have microsatellite instability.

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.

OTHER KEY ATTRIBUTES

Weekly GI and Liver Tumor Boards: Newly diagnosed patients with GI cancers who might benefit from multi-disciplinary consultation are seen in the weekly GI or Liver Tumor Boards. These tumor board teams include medical oncologists, surgical oncologists, radiation oncologists, interventional and diagnostic radiologists, nuclear medicine specialists, gastroenterologists, and pathologists. Anyone with localized esophageal, gastric, pancreas, rectal or anal 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.

Neuroendocrine Tumor (NET) Program: Stanford is a high volume referral center for these rare cancers and will formally launch a NET Program in Spring 2016. This program will bring together clinical and research expertise in areas such as medical oncology, surgical oncology, interventional radiology, nuclear medicine, endocrinology and survivorship. Stanford has contributed to key clinical trials in this field that will likely lead to the FDA-approval of new drugs for patients with NETs, including telotristat, an oral inhibitor of serotonin synthesis, and peptide receptor radionuclide therapy.

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 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.

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.

NEW FACULTY

We are pleased to introduce Dr. Sigurdis (Sisi) Haraldsdottir, the newest addition to the GI Medical Oncology Program. Dr. Haraldsdottir completed medical school at the University of Iceland and residency in Internal Medicine at the Landspitali University Hospital, Iceland, before moving to the United States. She completed a second residency in Internal Medicine at Boston University followed by a fellowship in Medical Oncology at Ohio State. She is currently pursing a PhD in Epidemiology and Cancer Genetics. She brings special expertise in the area of Lynch Syndrome (HNPCC) and colorectal cancer and will make important contributions to the program.

CLINICAL TRIALS INCLUDE

Genomic

Mixed Solid Tumors

- My Pathway: An Open-Label Phase IIA Study Evaluating Trastuzumab/Pertuzumab, Erlotinib, Vemurafenib, and Vismodegib in Patients Who Have Advanced Solid Tumors with Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents (VAR0115)

Pancreas

- A Phase 3, Randomised, Double Blind, Placebo Controlled, Multicentre Study of Maintenance Olaparib Monotherapy in Patients with gBRCA Mutated Metastatic Pancreatic Cancer whose Disease Has Not Progressed on First Line Platinum Based Chemotherapy (PANC0018)

Colon/Rectal Adenocarcinoma

Neoadjuvant Rectal

- A Phase 2/3 Trial of Neoadjuvant FOLFOX with Selective Use of Combined Modality Chemoradiation versus Preoperative Combined Modality Chemoradiation for Locally Advanced Rectal Cancer Patients Undergoing Low Anterior Resection with Total Mesorectal Excision (ECOGN1048)

Metastatic 1st Line

- SOON TO OPEN: A Phase 3 Study of Pembrolizumab vs. Chemotherapy in MSI H or Mismatch Repair Deficient Stage IV Colorectal Cancer (Keynote-177) (COR0016)

Metastatic 2nd Line

- SOON TO OPEN: A Randomized Phase 2 Study of Irinotecan and Cetuximab +/- Ramucirumab in Advanced K-ras WT Colorectal cancer Following Progression on Bevacizumab (ECOG-ACRIN-E7208)

Metastatic ≥ 3rd Line

- A Phase 3 Double- Blinded-Placebo controlled Study of Xilonix for Improving Survival in Metastatic Colorectal Cancer (COR0011)
- A Phase 2 Randomized, Open-Label Study of RRx-001 vs Regorafenib in Subjects with Metastatic Colorectal Cancer (COR0012)
- A Phase Ib Study of the Safety and Pharmacology of MPDL3280A Administered with Cobimetinib in Patients with Locally Advanced or Metastatic Solid Tumors (including colorectal) (VAR0103)
- Phase 2 Study of MK-3475 in Patients with Microsatellite Unstable (MSI) Tumors (VAR0107)

Gastroesophageal Adenocarcinoma

Metastatic

- SOON TO OPEN: A Phase 2 Study of Pembrolizumab and Epacadostat in Advanced Gastroesophageal Cancer
- SOON TO OPEN: A Phase 1b/2 Study of MEDI4736 (Anti PD-L1) in Combination with Tremelimumab (Anti-CTLA4), MEDI4736 Monotherapy, and Tremelimumab Monotherapy in Subjects with Metastatic or Recurrent Gastric or Gastroesophageal Junction Adenocarcinoma (GI0012)

Hepatocellular Carcinoma

- A Phase 3 Prospective, Randomized, Blinded and Controlled Investigation of Hepasphere/Quadrasphere Microspheres for Delivery of Doxorubicin for the Treatment of Hepatocellular Cancer (HEP0038)

Neuroendocrine/Carcinoid Tumors

Metastatic Pancreatic NET

- A Phase 2 Study of Capecitabine, Temozolomide and Bevacizumab for Metastatic or Unresectable Pancreatic Neuroendocrine Tumors (NET0012)
- A Randomized Phase 2 Study of Temozolomide or Temozolomide and Capecitabine in Patients with Advanced Pancreatic Neuroendocrine Tumors (ECOGE2211)
- SOON TO OPEN: Phase 1, Multicenter, Cohort Dose Escalation Trial to Determine the Safety, Tolerance, and Maximum Tolerated Dose of DCR-MYC, a Lipid Nanoparticle (LNP)-Formulated Small Inhibitory RNA (siRNA) Oligonucleotide Targeting MYC, in Patients with Refractory Locally Advanced or Metastatic Solid Tumor Malignancies, Multiple Myeloma, or Lymphoma (NET0021)

Metastatic Carcinoid

- A Phase 1, Open-label, Dose-escalation Study of SNX-5422 and Everolimus in Subjects with Neuroendocrine Tumors (VAR0120)
- A Prospective Randomized Phase 2 Trial of Pazopanib (NSC # 737754, IND 75648) versus Placebo in Patients with Progressive Carcinoid Tumors (ECOGA021202)
- SOON TO OPEN: A Prospective, Randomized, Double-Blind, Multi-Center, Phase II Study of the Efficacy and Safety of Lanreotide Autogel/ Depot 120 mg vs. Placebo for Tumor Control in Patients with well Differentiated, Advanced Lung or Thymus Neuroendocrine Tumors (NET0022)
- SOON TO OPEN: Randomized Phase II Study of Cisplatin and Etoposide versus Temozolomide and Capecitabine in Patients with Advanced G3 Non-Small Cell Gastroenteropancreatic Neuroendocrine Carcinomas (ECOG-ACRIN-EA2142)

Pancreatic Adenocarcinoma

Locally Advanced

- A Randomized Phase 3 Study Evaluating Modified FOLFIRINOX (mFFX) with or without Stereotactic Body Radiotherapy (SBRT) in the Treatment of Locally Advanced Pancreatic Cancer (PANC0015)
- SOON TO OPEN: A Randomized Multi-Center Study Comparing No Drainage to Preoperative Biliary Drainage Using Metal Stents in Patients with Resectable Pancreatic or Periampullary Cancer (PANC0021)

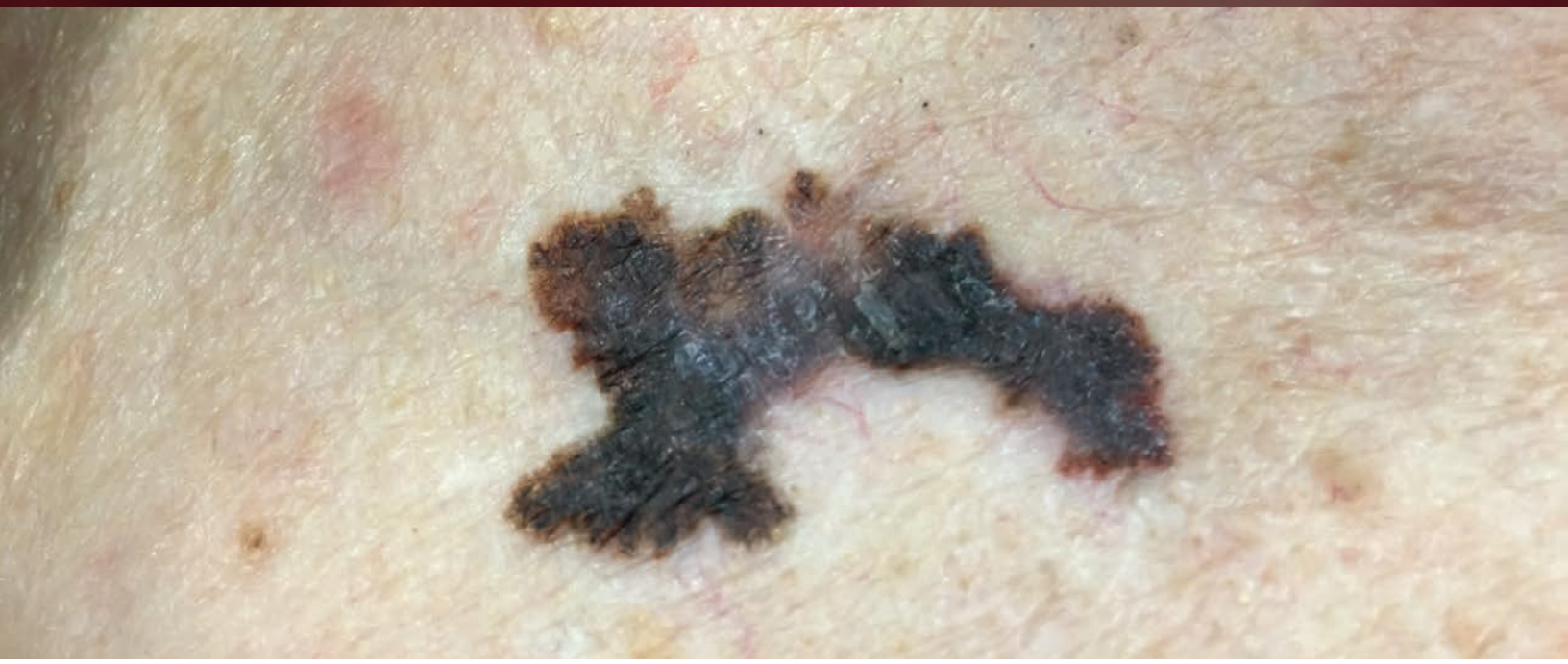
Metastatic

- A Phase 1/2 Study of Indoximod in Combination with Gemcitabine and Nab-Paclitaxel in Patients with Metastatic Adenocarcinoma of the Pancreas (METS0001)
- A Randomized Phase 2 Study of the Safety, Efficacy, and Immune Response of GVAX Pancreas Vaccine (with Cyclophosphamide) and CRS-207 with or without Nivolumab in Patients with Previously Treated Metastatic Pancreatic Adenocarcinoma (PANC0019)
- SOON TO OPEN: A Phase 1b/2 Open-Label, Multicenter Study of MEDI4736 Evaluated as a Single Agent or in Different Combinations in Patients with Metastatic Pancreatic Ductal Adenocarcinoma (EVEREST) (PANC0023)
- SOON TO OPEN: A Phase 2 Open-Label, Multicenter Study of MEDI4736 Evaluated as Single Agent or in Combination with Tremelimumab in Patients with Metastatic Pancreatic Ductal Adenocarcinoma (ALPS) (PANC0022)

- *highlighted studies are Stanford investigator initiated*

Stanford Cutaneous Oncology

Skin Cancer Program in Solid Tumors



Providing: Innovative Prevention, Treatment and Novel Therapy for Patients with Pigmented Lesions and Melanoma, Basal Cell Carcinoma, High-Risk Squamous Cell Carcinoma, and Merkel Cell Carcinoma, as well as Supportive Dermato-Oncology

The Skin Cancer Program at the Stanford Cancer Institute is a leading innovator in the research and treatment of all types of skin cancer, including melanoma and atypical melanocytic neoplasms (both adult and pediatric), high-risk and solid organ transplant-associated squamous cell carcinoma, advanced basal cell carcinoma, Merkel cell carcinoma and rarer cutaneous adnexal malignancies. It encompasses several distinct clinical programs and is led by Dr. Susan Swetter, Professor of Dermatology/Cutaneous Oncology. Clinics are held in the Stanford Cancer Center in Palo Alto and the Cancer Center South Bay (CCSB) facility in San Jose.

RECENT CUTANEOUS ONCOLOGY PROGRAM EXPANSION HIGHLIGHTS

New Faculty, Program Development, and Community Outreach

The Cutaneous Oncology Program welcomed both Dr. **Teresa Fu** and Dr. **Dana Lin** to the care team in September 2015.

Dr. Fu is Clinical Assistant Professor of Dermatology, having completed her dermatology residency and chief residency at Stanford in July 2015. Dr. Fu specializes in the multidisciplinary care of patients with Merkel cell carcinoma and high-risk and solid organ transplant-associated squamous cell carcinoma (SCC). She recently took over direction of the **Post-Transplant/High Risk Skin Cancer Clinic** from Dr. Cari Lee, who will be continuing her SCC-related research and clinical care of nonmelanoma skin cancer patients in early 2016 as Assistant Professor of Dermatology at the VA Palo Alto Health Care System. Dr. Fu sees patients at the 900 Blake Wilbur 3rd Floor location in Palo Alto (BW-3), as well as in the new Stanford CCSB location in San Jose.

The Stanford Pigmented Lesion and Melanoma Program (PLMP) welcomed Dr. **Dana Lin**, Clinical Assistant Professor of Surgery as the newest melanoma and Merkel cell carcinoma surgeon. Dr. Lin completed her general surgical and fellowship training

on the East Coast at Rutgers Robert Wood Johnson Medical School and the Massachusetts General Hospital. She specializes in sentinel lymph node biopsy and lymphadenectomy for trunk and extremity melanoma. While currently based in the PLMP in Palo Alto, Dr. Lin plans to expand her practice to the Stanford CCSB facility in early 2016. Dr. Lin also has clinical expertise and research interests in endocrine surgery and surgical education.

Dr. **Kavita Sarin**, Clinical Assistant Professor of Dermatology, developed a Skin Cancer Genetic Clinic in BW-3 to treat patients at high risk of skin cancer due to strong family history or positive genetic test results. This clinic provides preventive care, skin surveillance and education to at-risk patients, in conjunction with Stanford Cancer Genetics faculty and counselors. Patients include those with the p16/CDKN2A mutation associated with melanoma and pancreatic cancer, as well as inherited cancer syndromes such as Li- Fraumeni, familial melanoma and pancreatic cancer, BRCA1 and BRCA2, neurofibromatosis, and Lynch Syndrome.

Dr. **John Yost**, Clinical Assistant Professor of Dermatology initiated a novel Nail Disorders Clinic within the Stanford Cancer Center in Palo Alto, focused on treating debilitating nail-related side effects from cancer therapy and improving diagnosis and treatment of skin cancers, including melanoma, that arise within the nail unit. Conditions treated include paronychia and onychocryptosis resulting from EGFR-inhibitor therapy, onycholysis associated with chemotherapeutic agents, secondary bacterial and fungal infections of the nail unit from therapy-related immunosuppression, and treatment and monitoring of longitudinal melanonychia and other neoplastic onychodystrophies.

In July 2015, Clinical Assistant Professor of Dermatology Dr. **Silvina Pugliese** expanded the **Supportive Dermato-Oncology (SDO) Program** to the CCSB in San Jose. This unique service, which was developed by Stanford Clinical Assistant Professor Dr. **Bernice Kwong** in 2012, allows for same-day, on-site dermatology evaluation of patients undergoing cancer therapy to address cutaneous complications related to cancer diagnosis and treatment, allowing for improved quality of life during therapy. Dr. Kwong is spearheading the new Dermatology-Oncology Consult Service (DOCS) to provide dedicated SDO services to cancer inpatients at Stanford Hospital, slated to begin this year. Dr. **S. Tyler Hollmig**, Clinical Assistant Professor of Dermatology and Director of Laser and Aesthetic Dermatology has established an "Aesthetic Oncology" practice in Stanford Dermatology to provide additional care for cancer patients with treatment-related aesthetic concerns.

In 2014, Professor of Dermatology Dr. **Sumaira Aasi** along with Dr. **Vasu Divi**, Assistant Professor of Otolaryngology, Head and Neck Surgery, established a multi-specialty **Nonmelanoma Skin Cancer Working Group**, which includes over 20 Stanford faculty members in the departments of medical and surgical dermatology, dermatopathology, head and neck and plastic/reconstructive surgery, medical and radiation oncology, as well as basic science and translational researchers. This monthly "dry" Tumor Board examines optimal treatment for patients with advanced basal cell carcinoma (BCC), high-risk SCC, and other rare skin tumors, and promotes translational research.

Associate Professor of Dermatology Dr. **Anne Chang** works with Stanford medical and surgical oncology specialists to provide a weekly multidisciplinary Advanced Basal Cell Carcinoma (BCC) Clinic at BW-3. Together, they collaborate in the care of patients with complex and difficult-to-treat BCCs referred from the surrounding region and other states.

CUTANEOUS MALIGNANCIES — CLINICAL AND TRANSLATIONAL RESEARCH HIGHLIGHTS

- **New Immunotherapy Trials**

  The novel immunotherapy agent targeting PD-1 is being tested in a phase 2 trial at Stanford as a treatment for advanced Merkel cell carcinoma. Stanford radiation and medical oncologists analyzed the first cohort of patients in the pilot trial of ipilimumab and palliative radiation therapy for metastatic melanoma, in which significant clinical

responses in disease sites outside the radiation therapy field were observed in a subset. A phase 1 trial of combination checkpoint blockade (ipilimumab and nivolumab) and radiation therapy is slated to begin at Stanford under the direction of Dr. **Susan Knox**, Associate Professor of Radiation Oncology, and collaborating institutions. Stanford neuro-oncologists have been leading a phase 2 trial of nivolumab (PD-1 inhibitor) and ipilimumab for melanoma with brain metastasis. Additional early phase trials of PD-1 inhibitors as in combination with other agents are also being studied at Stanford for melanoma and other skin cancer types, under the direction of Dr. **Shivaani Kummar**, Professor of Medicine and Director, Phase I Clinical Research Program, in the Division of Oncology at Stanford. Dr. **John Sunwoo**, Associate Professor of Otolaryngology (Head and Neck Surgery) continues his translational research to explore differences in immune responses to cancer between men and women. Numerous high-impact scientific publications have resulted from the collaborative research efforts of the Stanford Cutaneous Oncology faculty and staff that will advance the care and survivorship of cancer patients.

- **Novel Medical Therapy for Basal Cell Carcinomas**
  The Basal Cell Carcinoma Research Group at Stanford is conducting ongoing clinical studies to assess novel therapies for patients with aggressive and/or inoperable BCC, as part of the Nonmelanoma Skin Cancer Program. This research includes:
  - Testing chemoresistant BCCs with combination therapies.
  - Studying ways to improve quality of life of patients while on long term targeted chemotherapy.

CLINICAL TRIALS INCLUDE

Melanoma

- A Pilot Study of Ipilimumab in Subjects with Stage IV Melanoma Receiving Palliative Radiation Therapy (MEL0005)
- A Phase 1b, Open-label, Multicenter, Dose-escalation Trial of Intratumoral Injections of SD-101 in Combination with Pembrolizumab in Patients with Metastatic Melanoma (METS0003)
- A Phase 1/2 Dose Escalation and Cohort Expansion Study of the Safety and Tolerability of Urelumab Administered in Combination with Nivolumab in Advanced /Metastatic Solid Tumors and B Cell Non-Hodgkins Lymphoma (VAR0126)
- A Multi-Center Phase 2 Open-Label Study to Evaluate Safety and Efficacy in Subjects with Melanoma Metastatic to the Brain Treated with Nivolumab in Combination with Ipilimumab Followed by Nivolumab Monotherapy (BRN0027)
- SOON TO OPEN: A Phase I Study to Evaluate the Safety and Efficacy of Combination Checkpoint Blockade (Ipilimumab and Nivolumab) Plus External Beam Radiotherapy in Subjects with Stage IV Melanoma (MEL0015)
- SOON TO OPEN: A Phase 3 Randomized Trial of Dabrafenib and Trametinib Followed by Ipilimumab and Nivolumab or Ipilimumab and Nivolumab Followed by Dabrafenib and Trametinib in Treating Patients with Stage III-IV BRAFV600 Melanoma (EA6134)
- SOON TO OPEN: A Phase III Randomized Trial Comparing High-Dose Interferon to Pembrolizumab in Patients with High Risk Resected Melanoma. (SWOGS1404)

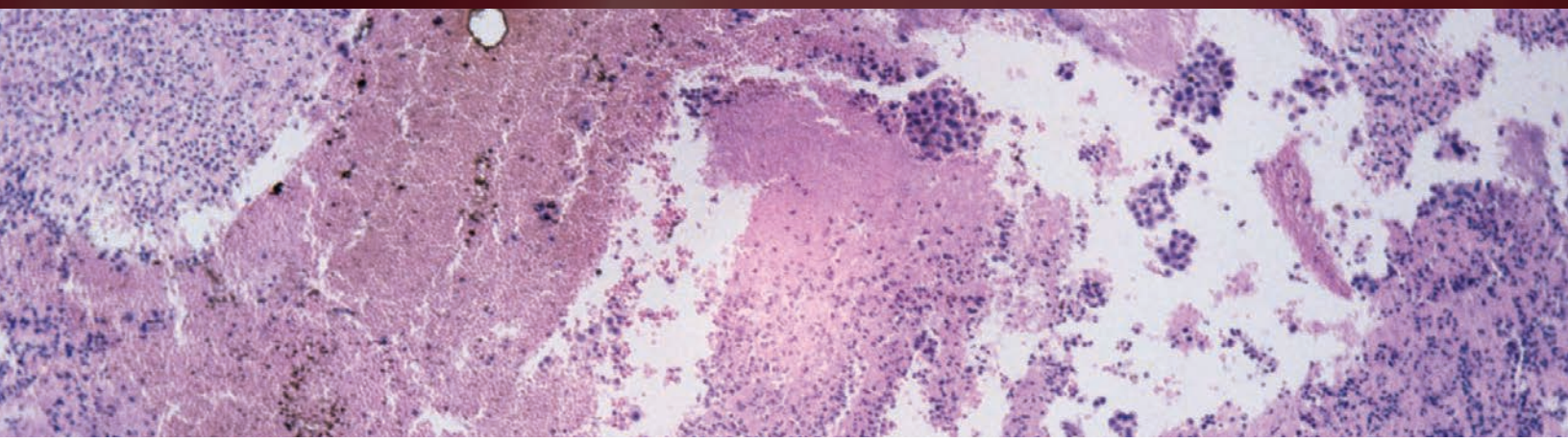
Nonmelanoma Skin Cancer

- Double-Blind, Randomized, Placebo-Controlled Two-Period Crossover Study to Assess the Effect of L-Carnitine on Vismodegib-Associated Muscle Spasms (SKIN0018)
- An Open-Label Pilot Study to Evaluate the Efficacy and Safety of a Combination Treatment of LDE225 and BKM120 for the Treatment of Advanced Basal Cell Carcinomas (SKIN0020)
- A Phase II Study of MK-3475 in Patients with Advanced Merkel Cell Carcinoma (MCC) (SKIN0025)
- Oral Arsenic Trioxide and Itraconazole for the Treatment of Patients with Advanced Basal Cell Carcinoma (SKIN0028)
- A Case Study of the Effects of Topical Itraconazole on Pharmacodynamic Modulation of Hedgehog Target Gene Expression in BCC in Patients (SKIN0030)

- *highlighted studies are Stanford investigator initiated*

Developmental Therapeutics

Phase I and II Clinical Research Program for Multiple Cancers



Stanford Cancer Center's Developmental Therapeutics (DT) Program, led by director Shivaani Kummar, MD, offers Phase 1/ 2 clinical trials designed to evaluate new treatment for cancer. Other faculty participating in this effort include Drs. Heather Wakelee and Joel Neal (lung cancers), A. Dimitrios Colevas (head and neck cancers), George Fisher and Pamela Kunz (GI cancers), George Sledge, Suleiman Massarweh, Mark Pegram and Melinda Telli (breast cancers), Sunil Reddy (melanoma), Ranjana Advani (lymphomas), and Branimir I. Sikic.

DT Program Director Dr. Kummar is a Professor of Medicine in the Stanford Division of Oncology and former leader of the National Cancer Institute's Developmental Therapeutics Clinic and Early Clinical Trials Development Program. Dr. Kummar's research interests focus on developing novel therapies for cancer. She specializes in conducting pharmacokinetic and pharmacodynamic driven first-in-human trials tailored to make early, informed decisions regarding the suitability of novel molecular agents for further clinical investigation. Her studies integrate genomics and laboratory correlates into early phase trials, establishing the proof of mechanism and proof-of-concept in these trials. She has published numerous articles in medical journals and serves on a number of national and international scientific committees.

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. The program offers the opportunity for patients to enroll in clinical trials evaluating novel anticancer therapies. The overall goal of the program is to facilitate the development of promising, new treatments for cancer while ensuring the highest standards of patient safety.

Below is a sampling of currently available Phase I and II studies.

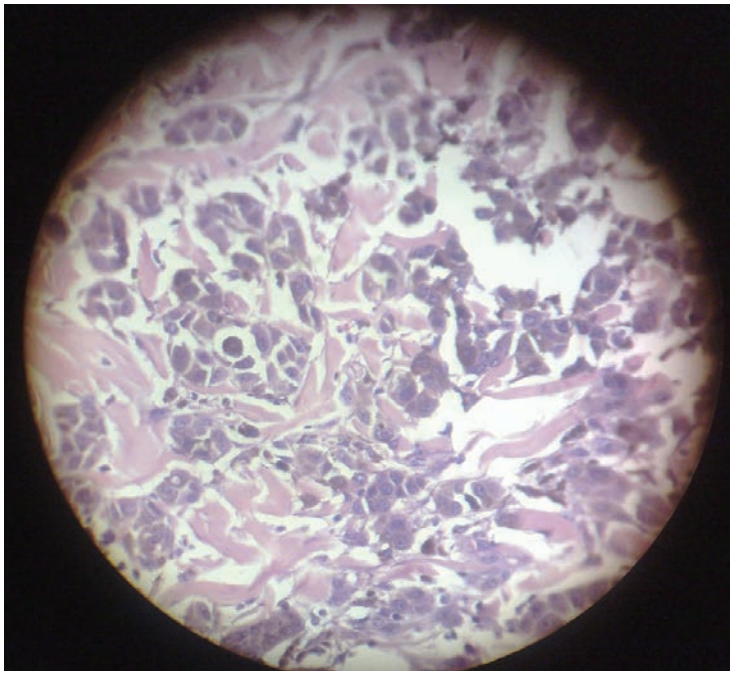
PHASE I AND II STUDIES

Multiple Solid Tumor Sites

- A Phase 1b, Open-label, Multicenter, Dose-escalation Trial of Intratumoral Injections of SD-101 in Combination with Pembrolizumab in Patients with Metastatic Melanoma (METS0003)
- A Phase 1/2 Dose Escalation and Cohort Expansion Study of the Safety and Tolerability of Urelumab Administered in Combination with Nivolumab in Advanced/Metastatic Solid Tumors and B Cell Non-Hodgkins Lymphoma (VAR0126)
- A First-In-Human Phase 1, Dose-Escalation, Safety and Pharmacokinetic Study of PF-06647020 in Adult Patients with Advanced Solid Tumors

Stanford Sarcoma Program

Targeted Therapies, Radiation Treatment, New Cutting Edge Drug Trials



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 aldoxorubicin and regorafenib. 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, 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

- PLX108-10: A Double-blind, Randomized, Placebo-controlled Phase 3 Study of Orally Administered PLX3397 in Subjects with Pigmented Villonodular Synovitis or Giant Cell Tumor of the Tendon Sheath (SARCOMA0018)
- Pilot Study to Explore the Role of Circulating Tumor DNA in the Management of Patients with Soft Tissue Sarcoma (SARCOMA0016)
- A Phase 1/2 Study of FPA008, an Anti-CSF1 Receptor Antibody, in Patients with Pigmented Villonodular Synovitis (PVNS)/Diffuse Type Tenosynovial Giant Cell Tumor (dt-TGCT) (SARCOMA0019)
- A Blanket Protocol to Study Oral Regorafenib in Patients with Refractory Liposarcoma, Osteogenic Sarcoma, and Ewing/Ewing-Like Sarcomas (SARC-024)
- A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial of Doxorubicin plus Olaratumab versus Doxorubicin plus Placebo in Patients with Advanced or Metastatic Soft Tissue Sarcoma (METS0004)
- A Feasibility Study to Evaluate the Safety and Effectiveness of ExAblate Magnetic Resonance Imaging Guided High Intensity Focused Ultrasound Treatment of Soft Tissue Tumors of the Extremities (VAR0095)
- A Phase 2 Multi-Center Investigation of Efficacy of ABI-009 (Nab-Rapamycin) in Patients with Advanced Malignant Perivascular Epithelioid Cell Tumors (PEComa) (SARCOMA0020)
- A Randomized, Open-Label, Phase 2 Trial of CMB305 (Sequentially Administered LV305 and G305) and Atezolizumab in Patients with Locally Advanced, Relapsed, or Metastatic Sarcoma Expressing NY-ESO-1 (SARCOMA0022)

- *highlighted studies are Stanford investigator initiated*

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