

# Clinical Research

Newsletter for Colleagues in the Community

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Welcome to our Fall 2017 issue. This quarterly publication is designed to inform our colleagues in the medical community about current clinical trials and research studies available at Stanford Cancer Institute, a National Cancer Institute-designated comprehensive cancer center. Many of these trials provide access to novel therapies including new “targeted” agents and immunotherapeutic options not available in the community.

As the leader of the Breast Cancer Clinical Research Group, I am delighted to have the opportunity to introduce this issue, which showcases our multi-disciplinary programs in Urologic Oncology, Gynecologic Oncology, and Breast Oncology. Each of these programs offers cutting-edge clinical trials for patients with tumors that can be challenging to treat with current routine care. Each program offers a multi-disciplinary tumor board so a team of experts can thoroughly review a patient’s record, imaging, and pathologic specimens to discuss all aspects of the patient’s condition. The reviews provide comprehensive treatment recommendations for the most complex of cases. This issue also profiles Stanford’s Clinical Cancer Genetics and Developmental Therapeutics programs.

Established in 2000, the Stanford Clinical Cancer Genetics Program is committed to detecting personal and familial genetic risk for cancer before the disease is diagnosed and becomes difficult to treat. With this focus, the Program provides consultative expertise for your referrals including patient diagnosis and management, and concentrates on clinical and translational research of inherited cancer, the incorporation of next-generation DNA sequencing technologies into genetic counseling and testing, and comprehensive cancer risk assessment and reduction for patients with hereditary cancer syndromes.

The Developmental Therapeutics Program focuses on developing novel therapies for cancer through first-in-human trials of

novel agents. These trials typically include pharmacokinetic, pharmacodynamics, and other translational correlates tailored to make early informed decisions regarding the suitability of novel molecular agents for further clinical investigation.

The Stanford Urologic Oncology Program features faculty with expertise in all aspects of the treatment of patients with cancers of the prostate, kidney, bladder, and testis. Care is tightly integrated with joint clinics and coordination between surgeons, medical oncologists, and radiation oncologists. This allows effective management of complex problems, with continuity in care along the entire course of the disease, from early diagnosis through management of advanced disease. Patients receive personalized, compassionate care with access to cutting-edge clinical trials and state-of-the-art surgical, medical, and radiation treatments.

The mission of the Stanford Women’s Cancer Center, home of the Gynecologic and Breast Oncology programs, is to provide the most outstanding comprehensive care for women with cancer. Breast program studies range from triple negative and hormone-dependent to HER2-positive disease, as well as brain metastases in breast cancer.

The Gynecologic program investigates novel immunotherapies for ovarian cancer as well as targeted therapies for gynecologic cancers.

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. You should also know that all of our highly specialized disease specific groups would be more than delighted to see your patients in second opinion visits, whenever the need arises, to help you in the most complex of cases.



**Suleiman Alfred Massarweh, MD**

*Associate Professor of Medicine*

*Leader, Breast Cancer Clinical Research Group (CRG)*

*Director, Medical Oncology Fellowship Program*

# Stanford Breast Cancer Research Program

A world-class group of researchers and clinicians

## AREAS OF INVESTIGATION AND HIGHLIGHTS

Our clinician investigators and researchers have dedicated their careers to studying breast cancer and our outpatient practice is exclusively dedicated to the treatment of patients with this disease. This high degree of specialization and diverse research backgrounds of our individual team members serve to create dedicated areas of research and clinical focus, which provides patients with a unique experience in getting the best advice possible for management of their disease. Our breast oncology group sees about 800 new breast cancer patients a year, many of whom were second opinion visits from you, our community partners, and we are privileged to continue to be part of your patients' experience and look forward to continuing this relationship to serve our community.

The Stanford breast cancer team is composed of world-class breast oncology specialists, with particular interests in different subsets of the disease. My own research for the past 15 years has been focused in the area of hormone receptor positive breast cancer and endocrine therapy; an area of research that has transformed our approach to treating women with metastatic hormone receptor positive breast cancer, but with much work that remains to be done, particularly in early disease. As such, a large part of my clinical practice is devoted to the treatment of women with endocrine-resistant metastatic disease and refractory breast cancer. In addition, I also have interests in treating women with breast cancer during pregnancy, breast cancer in men, and brain metastasis in breast cancer. Please don't hesitate to call anytime if you have a patient you think may benefit from a visit or a clinical trial at Stanford.

Dr. Melinda Telli, who is the co-leader of our breast cancer clinical research group, is a world-renowned expert in triple negative breast cancer (TNBC), and is a very active investigator in this area with a robust clinical trials portfolio for patients with recurrent triple-negative and hereditary breast cancer. In

metastatic TNBC, our current studies are exploring the anti-PD-L1 inhibitor atezolizumab, the ATR inhibitor VX-970, and the oral glutaminase inhibitor CB-839 all in combination with chemotherapy. In addition, the PARP inhibitor talazoparib is being investigated as a single agent in patients with "BRCA-like" metastatic TNBC, and we have an immunotherapy study of intratumoral plasmid IL-12 open for TNBC patients with chest wall or skin metastases. For recurrent hereditary breast cancers, we have studies exploring the role of the PARP inhibitor talazoparib in patients with BRCA1 and BRCA2 mutation-associated breast cancer, in addition to patients with inherited homologous recombination pathway gene mutations beyond BRCA1 and BRCA2, such as PALB2, ATM, RAD51, CHEK2, BRIP1, among others. We are also investigating the novel DNA damaging chemotherapeutic lurbinectedin (PM01183) in patients with recurrent BRCA1 and BRCA2 mutation-associated breast cancer.

Dr. Allison Kurian, who serves as the Director of the Women's Clinical Cancer Genetics Program, is world-renowned in the area of hereditary breast cancer and management of high-risk patients and has a robust breast cancer practice across disease settings.

Our group includes other prominent clinician researchers such as Dr. Mark Pegram, who is well known for his work in HER2-positive breast cancer, and Dr. George Sledge, who is a national leader in breast cancer research and treatment. Both Drs. Sledge and Pegram provide essential leadership and vision for our breast group.

These are just key highlights of our breast research group, with many other productive and engaged members across disease disciplines involved in breast cancer. The diversity of our group provides a unique opportunity for interaction in our daily practice and weekly patient care conference (Tumor Board) as well as always exploring new research ideas through regular interactions with scientists across the Stanford

campus and other researchers in other institutions to always provide the most cutting-edge research to our patients.

In addition to the clinical trials highlighted below, our breast group interacts closely with the newly established Stanford Phase I Drug Development Program, which provides expanded patient access to early stage and first-in-human novel therapeutic clinical trials.

## HIGHLIGHTS OF CURRENT THERAPEUTIC STUDIES

### Adjuvant Therapy

- A Phase III Study Evaluating Palbociclib (PD-0332991), a Cyclin-Dependent Kinase (CDK) 4/6 Inhibitor in Patients with Hormone-Receptor-Positive, HER2-Normal Primary Breast Cancer with High Relapse Risk After Neoadjuvant Chemotherapy - "PENELOPE B" (NSABPB54)  
*This study is exploring one year of palbociclib vs. placebo in hormone receptor-positive, HER2-negative breast cancer with residual disease following ≥16 weeks of neoadjuvant chemotherapy.*
- A Randomized, Double-Blind, Parallel Group, Placebo-Controlled Multi-Centre Phase III Study to Assess the Efficacy and Safety of Olaparib Versus Placebo as Adjuvant Treatment in Patients with Germline BRCA1/2 Mutations and High Risk HER2 Negative Primary Breast Cancer Who Have Completed Definitive Local Treatment and Neoadjuvant or Adjuvant Chemotherapy (ECOGB55)  
*This study is exploring one year of olaparib vs. placebo in patients with early stage BRCA1/2 mutation-associated breast cancer following at least 6 cycles of (neo)adjuvant chemotherapy.*
- A Randomized Phase III Trial of Adjuvant Therapy Comparing Doxorubicin Plus Cyclophosphamide Followed by Weekly Paclitaxel with or without Carboplatin for Node-Positive or High-Risk Node-Negative Triple-Negative Invasive Breast Cancer (NRGBR003)  
*This study is evaluating the contribution of carboplatin to standard anthracycline and taxane-based adjuvant chemotherapy in Stage II-III TNBC.*
- PALLAS: PALbociclib CoLLaborative Adjuvant Study: A Randomized Phase III Trial of Palbociclib with Standard

Adjuvant Endocrine Therapy Versus Standard Adjuvant Endocrine Therapy Alone for Hormone Receptor Positive (HR+) / Human Epidermal Growth Factor Receptor 2 (HER2)-Negative Early Breast Cancer (ECOG-ACRIN-PRE0109)

*This study is comparing any positive and negative effects of using 2 years of Palbociclib in combination with standard anti-hormone therapy to using standard anti-hormone therapy alone and to evaluate the likelihood that invasive breast cancer returns.*

### Brain Metastases

- A Phase II Study of Etirinotecan Pegol (NKTR-102) in Patients with Refractory Brain Metastases and Advanced Lung Cancer or Metastatic Breast Cancer (MBC)  
*This study is investigating the efficacy of etirinotecan pegol for treatment of patients with brain metastases from breast cancer.*

### Breast Cancer Imaging Protocols

- Pilot Study of Technologies for Augmented Reality Breast Surgery (BRS0073)  
*This study is investigating how accurately a new system we have developed called "augmented reality display of breast magnetic resonance images" can reveal the extent of breast cancer immediately prior to surgery.*
- Magnetic Resonance Imaging of Breast Cancer (BRSNSTU0004)  
*This study is comparing magnetic resonance imaging with more well established diagnostic imaging techniques to determine which method best finds and defines breast cancer.*
- Breast Interstitial Fluid (BRS0060)  
*This study is investigating how proteins in breast interstitial fluid reflect the tissue environment and differ in areas near benign masses, malignant masses and normal tissue.*
- <sup>64</sup>Cu-DOTA-B-Fab as a PET Tracer for Evaluating CA6 Expression in Tumors: a First in Human Study (GYNOVA0033)  
*This study is investigating the use of copper Cu <sup>64</sup>-DOTA-B-Fab positron emission tomography (PET)/computed tomography (CT) in imaging patients with breast and ovarian cancer and in helping to potentially identify CA6 positive tumors.*
- <sup>18</sup>F FPPRGD2 PET/CT or PET/MRI Imaging of αvβ3 (alpha-v-beta-3) Integrins Expression as a Biomarker of Angiogenesis (VARIMG0002)  
*This study is investigating a new PET radiopharmaceutical in breast and other cancers requiring antiangiogenesis treatment.*

### Metastatic–BRCA 1/BRCA 2 Mutation

- A Multicenter Phase II Clinical Trial of PM01183 in BRCA1/2-Associated or Unselected Metastatic Breast Cancer (BRSMTS0022)

*PM01183 or lurbinectedin is a novel marine-derived DNA damaging chemotherapeutic being explored in BRCA1/2 mutation-associated breast cancer, including in platinum resistance.*

### Metastatic–Genomic

- A Phase II Basket Study of the Oral TRK Inhibitor LOXO-101 in Subjects with NTRK Fusion-Positive Tumors (VAR0136)

*This study is investigating LOXO-101 (Larotrectinib) in patients with advanced solid tumors harboring a fusion of NTRK1, NTRK2 or NTRK3.*

- A Phase II Clinical Trial of Talazoparib (BMN 673) in BRCA1 and BRCA2 Wild-Type Patients with (i) Advanced Triple-Negative Breast Cancer and Homologous Recombination Deficiency as Assessed by the HRD Assay, and (ii) Advanced HER2-Negative Breast Cancer with Either a Germline or Somatic Mutation in Homologous Recombination Pathway Genes (BRS0050)

*This study is examining the role of PARP inhibition beyond BRCA1 and BRCA2. Gene mutations of interest include: PTEN, PALB2, CHEK2, ATM, NBN, BARD1, BRIP1, RAD50, RAD51C, RAD51D, MRE11, ATR, Fanconi anemia complementation group of genes (FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL).*

- Molecular Analysis for Therapy Choice (MATCH) (ECOG-ACRIN-EAY131)

*This study is investigating how well treatment that is directed by genetic testing works in patients with solid tumors that have progressed following at least one line of standard treatment or for which no agreed upon treatment approach exists.*

### Metastatic–Genomic, HER2 Mutations

- A Phase II Study of Neratinib Alone and in Combination with Fulvestrant in Metastatic HER2 Non-amplified but HER2 Mutant Breast Cancer (BRS0033)

*This study is investigating the oral tyrosine kinase inhibitor neratinib in HER2 mutant advanced breast cancer.*

### Metastatic–HER2-Positive Disease

- A Phase I Multicenter, Open-Label, Dose-Escalation, and Dose-Expansion Study to Evaluate the Safety, Pharmacokinetics, Immunogenicity, and Antitumor Activity of MEDI4276 in Subjects with Select HER2-expressing Advanced Solid Tumors (VAR0128)

*MEDI4276 is a novel HER2 targeted antibody-drug conjugate being evaluated in advanced, refractory HER2-positive breast cancer.*

- Margetuximab Plus Chemotherapy vs. Trastuzumab Plus Chemotherapy in the Treatment of HER2+ Metastatic Breast Cancer (SOPHIA) (BRSMTS0024)

*This study is exploring a novel HER2 targeted monoclonal antibody combined with chemotherapy in HER2-positive patients previously treated with trastuzumab, pertuzumab and TDM1.*

### Metastatic–Triple-negative Breast Cancer

- A Phase II Clinical Trial of Talazoparib (BMN 673) in BRCA1 and BRCA2 Wild-Type Patients with (i) Advanced Triple-Negative Breast Cancer and Homologous Recombination Deficiency as Assessed by the HRD Assay, and (ii) Advanced HER2-Negative Breast Cancer with Either a Germline or Somatic Mutation in Homologous Recombination Pathway Genes (BRS0050)

*This study is examining the role of PARP inhibition beyond BRCA1 and BRCA2. Gene mutations of interest include: PTEN, PALB2, CHEK2, ATM, NBN, BARD1, BRIP1, RAD50, RAD51C, RAD51D, MRE11, ATR, Fanconi anemia complementation group of genes (FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL).*

- Evaluation of Pharmacodynamic Effects of Intratumoral Delivery of Plasmid IL-12 Electroporation in Patients with Triple Negative Breast Cancer (BRS0054)

*This study is exploring an intratumoral immunotherapy approach for metastatic TNBC patients with accessible chest wall or skin metastases.*

- A Multicenter, Open-label, Phase II Study of Imprime PGG and Pembrolizumab in Subjects with Advanced Melanoma Failing Front-line Treatment with Checkpoint Inhibitors (CPI) or Triple Negative Breast Cancer (TNBC) Failing Front-line Chemotherapy for Metastatic Disease (BRSMTS0026)

*This study is investigating the effect of Imprime PGG when given together with pembrolizumab in the treatment of triple negative breast cancer or advanced melanoma.*

### Observational

- The IDEA Study (Individualized Decisions for Endocrine therapy Alone) A Prospective, Single-Arm Cohort Study of Patients Receiving Endocrine Therapy Alone (Without Radiotherapy) After Breast Conserving Surgery for Early-Stage, Post-Menopausal Breast Cancer Patients Whose Tumors Have Favorable Biologic Features (BRS0066)

*This study is investigating whether women ages 50 to 69 with a certain type of breast cancer can safely avoid radiation treatment after lumpectomy surgery.*

# Gynecologic Oncology Program

Advanced Research, Specialized Treatments, Supportive Services



The Stanford Gynecologic Oncology Program, part of the Stanford Women's Cancer Center, offers treatments and clinical trials that utilize combined modalities and include advanced surgical techniques for ovarian, fallopian tube, cervical, endometrial, and other cancers of the female reproductive system.

The Program is led by Oliver Dorigo, MD, PhD, Director and Associate Professor, Division Gynecologic Oncology; Director of the Gynecologic Oncology Clinical Care Program, the Clinical Research Group for Gynecologic Oncology Trials, and the Mary Lake Polan Gynecologic Oncology Research Laboratory, and Jonathan Berek, MD, MMS, Director of the Stanford Women's Cancer Center, and the Laurie Kraus Laboc Professor at Stanford School of Medicine.

The mission of the Division of Gynecologic Oncology is to provide the most excellent and comprehensive care for women with gynecologic cancers. The Program is committed to the development of novel therapeutic and diagnostic strategies that will improve the prognosis and quality of life for patients with gynecologic cancers. The ultimate goal is to establish Gynecologic Oncology services at Stanford as one of the world's leading institutions for the treatment of gynecologic cancer.

To accomplish this mission within the next few years, Dr. Dorigo and his colleagues are applying a multifaceted strategy. The Stanford Gynecologic Oncology Service has expanded its clinical services to various outreach sites, which include the South Bay Cancer Center and Good Samaritan Hospital in San Jose, and the Dominican Hospital in Santa Cruz. In addition, we have established a Women's Cancer Program at Stanford Health Care – ValleyCare in Pleasanton with two excellent gynecologic oncologists, Dr. Valerie Sugiyama and Dr. Trung Nguyen. Dr. Amer Karam is spearheading our outreach efforts as the Director of Outreach and Robotic Surgery in Gynecologic Oncology at Stanford, and the Associate Chief of the Division of Gynecologic Oncology. Dr. Diana English has by now established a robust clinical practice at the Stanford Women's Cancer Center as well as in the South Bay, and we are excited to welcome Dr. Elisabeth Diver from the gynecologic oncology fellowship program at Harvard.

## INNOVATIVE RESEARCH PROGRAMS

The research efforts in the Stanford Division of Gynecologic Oncology are focused on both basic and clinical science. Dr. Dorigo is directing the Mary Lake Polan Gynecologic Oncology Research Laboratory, which is studying novel immunotherapies for ovarian cancer. In addition, various clinical studies are conducted through the clinical research group that focuses on immunotherapies and targeted therapies for gynecologic cancers.

## RESEARCH PROGRAMS INCLUDE

- Understanding the role of the immune system in ovarian cancer to better develop novel therapies.
- Refined methods for imaging ovarian cancer and studying biological markers that may improve detection—a program that is particularly important because ovarian cancer seldom reveals itself through early symptoms. Characterization of intracellular signaling pathways revealing new ways to classify ovarian tumors.

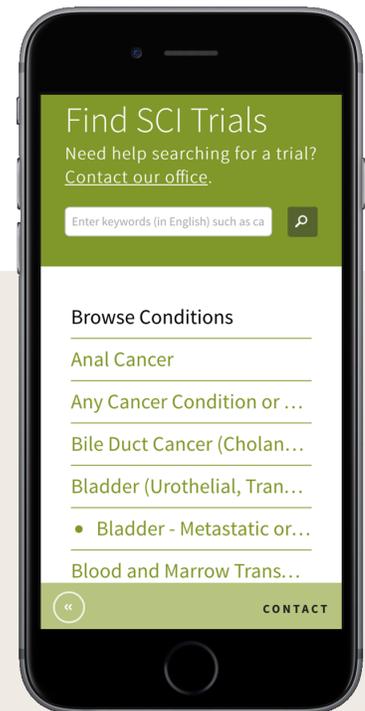
- Evaluation of the ability of therapeutic agents to help overcome chemotherapy resistance in ovarian cancers that appear to originate in stem cell-like cancer cells.
- Development of novel chemotherapies and investigations of fundamental biologic mechanisms of uterine tumors.

## SPECIAL CLINICAL PROGRAMS

- Multi-disciplinary Tumor Board. The Stanford Gynecologic Tumor Board includes gynecologic oncologists, radiologists, pathologists, nuclear medicine specialists, nurse specialists and genetic specialists. The weekly Tumor Board allows Stanford experts to provide a thorough and collaborative review of patient records, radiographs, and pathology results. Stanford is implementing videoconferencing to provide remote online access to Gynecologic Oncology Tumor Board discussion.
- Innovative treatments that combine modalities, including advanced surgical techniques and the most up-to-date chemotherapeutic agents.



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- Intraoperative radiation therapy (IORT).
- Fertility-conserving surgery and advanced assisted reproductive technology to help maximize childbearing options.
- A wide array of supportive services, focusing on psychological issues, sexual side effects, and changes in body image.
- The Stanford Survivorship Program, which offers unique supportive services for patients who have completed their treatment including surgery, radiation, and chemotherapy.

## CURRENT STUDIES INCLUDE

### Ovarian/Peritoneal/Fallopian

- A Phase I/II, Open-Label Safety and Efficacy Evaluation of CRS-207 in Combination with Epacadostat in Adults with Platinum-Resistant Ovarian, Fallopian, or Peritoneal Cancer (GYNOVA0038)
- A Phase 1b Study of an Immunotherapeutic Vaccine, DPX-Survivac with Low Dose Cyclophosphamide and Epacadostat (INCB024360) in Patients with Recurrent Ovarian Cancer (GYNOVA0039)
- 64Cu-DOTA-B-Fab as a PET Tracer for Evaluating CA6 Expression in Tumors: A First in Human Study (GYNOVA0033)

### Cervical

- Phase I Pilot Study to Evaluate the Prognostic Value of Perfusion CT for Primary Cervical Cancer (GYNCVX0003)

### Survivorship: Ovarian

- Feasibility Study of New Method of Diagnostic and Prediction of Painful Chemotherapy-induced Peripheral Neuropathy (CIPN) (GYN0006)

### Survivorship: Endometrial

- Step Into Wellness: A Program of Health and Recovery for Endometrial Cancer Survivors (GYNEND0002) (SOON TO OPEN)

### Recurrent Disease: Endometrial

- A Phase 2, Randomized Study of MLN0128 (a Dual TORC1/1 Inhibitor), MLN0128+MLN117 (a PI3Ka Inhibitor), Weekly Paclitaxel, or the Combination of Weekly Paclitaxel and MLN0128 in Women with Advanced, Recurrent, or Persistent Endometrial Cancer (GYNEND0001)

### Initial Therapy: Ovarian

- A Phase III, Multicenter, Randomized Study of Atezolizumab Versus Placebo Administered in Combination with Paclitaxel, Carboplatin, and Bevacizumab to Patients with Newly-Diagnosed Stage III or Stage IV Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (GOG3015)

### Initial Therapy: Endometrial

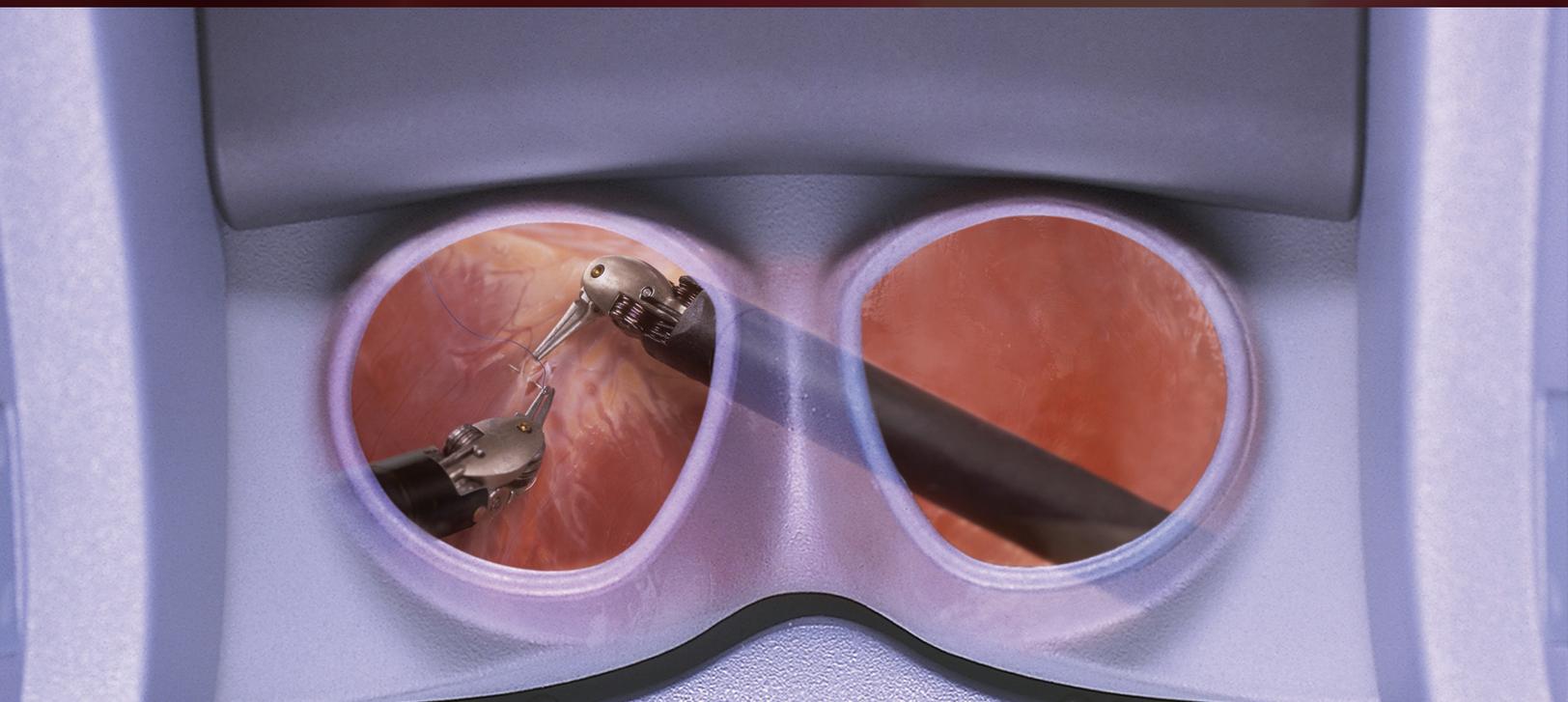
- A Randomized Phase II/III Study of Paclitaxel/Carboplatin/Metformin (NSC#91485) versus Paclitaxel/Carboplatin/Placebo as Initial Therapy for Measurable Stage III or IVA, Stage IVB, or Recurrent Endometrial Cancer (GOG0286B)

For more information on Gynecologic Oncology studies, contact: [GynOncResearch@stanford.edu](mailto:GynOncResearch@stanford.edu)

• *highlighted studies are Stanford investigator initiated*

# Urologic Oncology Program

Innovative Research, Treatments, Supportive Care



The Stanford Urologic Oncology Program features faculty with expertise in all aspects of the treatment of patients with cancers of the prostate, kidney, bladder, and testis. Care is tightly integrated with joint clinics and coordination between surgeons, medical oncologists, and radiation oncologists. This allows effective management of complex problems, with continuity in care along the entire course of the disease, from early diagnosis through management of advanced disease. Patients receive personalized, compassionate care with access to cutting-edge clinical trials and state-of-the-art surgical, medical, and radiation treatments.

The Program is led by Eila Skinner, MD, Chair of the Department of Urology and Thomas A. Stamey Research Professor in Urology, Stanford University Medical Center, and Sandy Srinivas, MD, Professor of Medicine (Oncology), Stanford University Medical Center. Dr. Skinner is a nationally known expert in urologic oncology with a special focus on the surgical management of bladder cancer and urinary tract reconstruction. Dr. Srinivas is a nationally known medical oncologist who is a panel member of the National Comprehensive Cancer Network and has research interests in prostate, renal, testis, and bladder cancer. The team

includes five urologic surgeons, three dedicated medical oncologists, two radiation oncologists who treat only urologic cancers, and a large support team of nurses, physician extenders, and research coordinators.

## STANFORD BREAKTHROUGHS IN UROLOGIC ONCOLOGY RESEARCH

Stanford has made scientific advances that support urologic cancer research. Some of these innovations include:

- DNA microarray technology that has enabled investigators to use miniscule quantities of tumor tissue to genetically

classify urologic cancers. Stanford scientists are identifying genomic signatures to better classify tumors as low or high risk, which may allow for improved recommendations regarding treatment.

- The MagSweeper, an automated device developed at Stanford, isolates and purifies cancer cells from blood with higher capture rates and purity. Used to study the genetic profiles of circulating cancer cells, this invention is the result of the collaboration between Stanford physicians and basic scientists.
- Leading-edge cancer stem cell research. Working with bladder cancer stem cells, Stanford scientists and clinicians will be targeting stem cells as a novel treatment for bladder cancer.
- Evaluation of improved imaging techniques for early detection and evaluation of response to therapeutics.
- Important discoveries in the hedgehog signaling pathway in solid tumors, which have led to novel investigational treatments for prostate cancer.
- Multiple breakthroughs in radiation therapy techniques applied to the treatment of prostate cancer dating back to the first linear accelerators, and including the development of IMRT and the CyberKnife

#### STANFORD UROLOGIC ONCOLOGY PROGRAM FEATURES

The Urologic Oncology Program includes a highly skilled team of individuals who exclusively focus on this area of oncology. The surgical team is adept at managing the most challenging minimally invasive and open cases. The medical team is highly experienced in treating urologic cancers and is using some of the most exciting and cutting-edge treatments available.

The team meets twice monthly in a multi-disciplinary tumor board that consists of medical, surgical, and radiation oncologists, as well as radiologists, pathologists, nurse coordinators, PAs, and research staff. This team of experts

thoroughly reviews patient records, imaging, and pathologic specimens, discusses all aspects of the patient's condition, and provides a comprehensive treatment recommendation.

Highlights of the state-of-the-art treatments for urologic cancers currently available at Stanford include:

- An individualized, risk-adapted strategy for treatment of early bladder, kidney, and prostate cancer to optimize the outcome for each patient.
- Management of complex patients with urinary tract malignancies, including providing chemotherapy and surgery for the very elderly, those with other significant medical problems, and those who have had prior treatment such as pelvic radiation or chemotherapy. This includes management of some of the most challenging cases in the field.
- Minimally invasive laparoscopic and robotic surgery for prostate, bladder, and kidney cancer. The surgical team has extensive experience with these surgeries and outstanding outcomes. This includes nerve-sparing prostatectomy and cystectomy and complex partial nephrectomy.
- Resection of complex locally-advanced kidney, bladder and testis cancers requiring a coordinated effort with a multidisciplinary surgical team.
- Urinary tract reconstruction with continent diversion and neobladder construction for many patients who require bladder removal for bladder cancer. The team has one of the largest experiences in the country in continent urinary diversion, and evaluates each cystectomy patient for the appropriateness of urinary reconstruction.
- Advanced imaging capabilities using new tracers for the detection of early and advanced disease.
- Immunotherapies such as Provenge for castration-resistant prostate cancer, high dose interleukin-2 for advanced renal cell carcinoma, and the new PD1 and PDL1 inhibitors for advanced kidney and bladder cancers.

- Clinical trials with novel therapeutics for early and advanced stage cancers of all types, including new biologic therapies.
- Focal therapy such as percutaneous cryoablation for small kidney cancers.
- Urologic cancer support group that holds monthly meetings offering lectures on state-of-the-art treatments, available clinical trials, and other patient care issues, and that conclude with an interactive panel discussion between the physicians and patients.
- Coordinated cancer survivorship program for long-term survivors of testis cancer treatment.

## CURRENT STUDIES INCLUDE

### Bladder

- A Phase III, Open-Label, Multicenter, Randomized Study of Atezolizumab (AntiPD-L1 Antibody) versus Observation as Adjuvant Therapy in Patients with PD-L1 Selected, High Risk Muscle Invasive Bladder Cancer after Cystectomy (BLDR0017)
- A Phase 2, Two-arm Multicenter, Open-Label Study to Determine the Efficacy and the Safety of Two Different Dose Regimens of a Pan-FGFR Tyrosine Kinase Inhibitor JNJ-42756493 in Subjects with Metastatic or Surgically Unresectable Urothelial Cancer with FGFR Genomic Alterations (BLDR0018)
- A Randomized Phase 2 Trial of Cisplatin/Gemcitabine with or without VX-970 in Metastatic Urothelial Carcinoma (BLDR0022)
- A Randomized Phase II Study of Co-Expression Extrapolation (COXEN) with Neoadjuvant Chemotherapy for Localized, Muscle-Invasive Bladder Cancer (ECOGS1314)

### Kidney

- A Phase 2 Randomized, Double-Blind Study of Dalantercept plus Axitinib Compared to Placebo plus Axitinib in Patients with Advanced Renal Cell Carcinoma (RENAL0030)
- A Phase I/II Study of the Safety, Pharmacokinetics, and Pharmacodynamics of the Glutaminase Inhibitor CB-839 in Combination with Nivolumab in Patients with Clear Cell Renal Cell Carcinoma and Other Solid Tumors (RENAL0035)

- A Multi-center, Open Label, Randomized Phase II Study of AGS-16C3F vs. Axitinib in Metastatic Renal Cell Carcinoma (RENAL0034)

### Prostate

- Quality of Life Following Radical Prostatectomy (PROS0012)
- Transrectal Photoacoustic Imaging of the Prostate (PROS0044)
- Photoacoustic Imaging (PAI) of the Prostate: A Clinical Feasibility Study (PROS0046)
- A Phase I Study Evaluating the Efficacy and Safety of Sodium Selenite in Combination with Palliative Radiation Therapy in Patients with Metastatic Cancer (PROS0047)
- Feasibility of Using Trans-Perineal Clarity Autoscan Ultrasound Imaging for Prostate Motion Management, Tissue Characterization, and Treatment Monitoring (PROS0055)
- A Phase I/II Study of High-Dose-Rate Brachytherapy as Monotherapy for Prostate Cancer (PROS0065)
- Focal MR-Guided Focused Ultrasound Treatment of Localized Intermediate Risk Prostate Lesions (PROS0067)
- 68Ga-RM2 PET/MRI in the Evaluation of Patients with Biochemical Recurrence of Prostate Cancer and Non-Contributory CT Scans (PROS0074)
- 68Ga-PSMA PET/MRI for Detection of Regional Nodal and Distant Metastases in Patients with Intermediate and High-Risk Prostate Cancer (PROS0075)
- 68Ga-PSMA PET/CT for Detection of Recurrent Prostate Cancer after Initial Therapy in Patients with Elevated PSA (PROS0076)

### Germ Cell

- Randomized Phase II Trial of Paclitaxel, Ifosfamide and Cisplatin (TIP) vs. Bleomycin, Etoposide and Cisplatin (BEP) for Patients with Previously Untreated Intermediate- and Poor-Risk Germ Cell Tumors (GCT0001)

### Seminoma

- Phase II Trial of Retroperitoneal Lymph Node Dissection as First-Line Treatment for Testicular Seminoma with Isolated Retroperitoneal Disease (1-3cm) (GU0002)

• *highlighted studies are Stanford investigator initiated*

# Clinical Cancer Genetics Program

Clinical and Translational Research, Genetic Counseling and Testing, Cancer Risk Assessment and Reduction



Established in 2000 as one of the first dedicated cancer genetics clinics on the West Coast, the Stanford Clinical Cancer Genetics Program is committed to detecting personal and familial genetic risk for cancer before the disease is diagnosed and becomes difficult to treat. With this focus, the Program provides consultative expertise for referred patient diagnosis and management, and concentrates on clinical and translational research of inherited cancer syndromes, the incorporation of next-generation DNA sequencing technologies into genetic counseling and testing, and comprehensive cancer risk assessment and reduction for patients with hereditary cancer syndromes. In addition, the Program provides educational outreach to health care professionals and the public.

The Stanford Clinical Cancer Genetics Program is led by James Ford, MD, Professor of Medicine and Genetics, in the Division of Oncology. Faculty members include Allison Kurian, MD, MSc, Associate Professor of Medicine and of Health Research and Policy, in the Divisions of Oncology and Epidemiology, who focuses on hereditary breast and ovarian cancers, and Uri Ladabaum, MD, MS, Professor of Medicine, in the Division of Gastroenterology, who focuses on hereditary GI cancers. Staff includes five full-time certified genetic counselors, a program manager, and a research assistant. Our three faculty are nationally recognized in their areas of cancer genetics and contribute regularly to writing guidelines

for genetic testing and screening for organizations such as the National Cancer Center Network, American Society for Clinical Oncology, American Gastroenterological Association, the International Hereditary Gastric Cancer Association, and others. Dr. Ford was recently named the founding editor-in-chief of the new ASCO sponsored journal JCO Precision Oncology, devoted to publishing cutting-edge research and commentary in this rapidly progressing field.

## CANCER GENETICS RESEARCH

The Stanford Cancer Genetics Program seeks to pinpoint genetic risks for hereditary cancer, create personalized cancer prevention, screening, and treatment strategies, and apply advances in personalized genomics to cancer prevention and treatment.

### Translational research features

- Breakthroughs in techniques to sequence multiple genes at a time (multi-gene panels), and the interpretation and application of these tests in the clinic, which is beginning to provide answers for families who test negative for mutations in single, highly penetrant genes such as **BRCA1/2** or **TP53**. The use of next-generation DNA sequencing, in the past too difficult or expensive, has become an essential tool in the clinic, and Stanford investigators are at the forefront of utilizing this technology and exploring its utility for genetic testing.
- Development of clinical protocols for the early detection and prevention of hereditary cancers. For example, the Program has a multi-disciplinary clinical protocol for genetic testing, screening, and prophylactic surgery for Hereditary Diffuse Gastric Cancer caused by **CDH1** mutations, and has become the primary referral center for this rare disorder in the US, allowing for the development of the Hereditary Gastric Cancer Registry.
- Clinical trials and early adopters of breast MRI for early detection of breast cancer in women at high genetic risk.

- “Universal” screening of all colorectal and endometrial cancers diagnosed and surgically resected at Stanford for defects in DNA mismatch repair proteins and microsatellite instability associated with Lynch syndrome (MSI-H). With the approval of immunotherapy drugs for treatment of MSI-high tumors, we are expanding our screening to all GI cancers and potentially all cancers, and investigating how many of these previously unrecognized tumors are part of familial Lynch syndrome.
- Sequencing and detection of mutations in circulating tumor DNA in individual’s serum as a highly sensitive screen for early hereditary cancers.
- Major research efforts involving the study of individuals and families with hereditary breast cancer. For example, using the unique populations in California, the Program has modeled breast cancer genetic risk due to **BRCA1/2** mutations across different racial/ethnic groups and tested these using collaborations with the Breast Cancer Family Registry (BCFR), and Hong Kong Breast Cancer Registry. Population-based studies are proceeding using multi-gene panels to determine the breast cancer risk associated with “moderate” penetrance gene mutations, such as those in the **ATM**, **PALB2**, **CHEK2** and **MRE11** genes.
- Creation of the “Decision Tool for Women with BRCA Mutations,” a decision analysis and outcomes tool to predict survival of women with **BRCA1/2** mutations based on various screening and prophylaxis interventions. This instrument was built and translated into a publicly available user-friendly website that has quickly gained wide use among cancer genetics professionals and patients to inform their clinical management. (To access this site, please visit [brcatool.stanford.edu](http://brcatool.stanford.edu))
- Translation of the Program’s laboratory expertise in DNA repair mechanisms into therapeutic trials of novel agents, including poly (ADP-ribose) polymerase (PARP) inhibitors for triple-negative breast cancer, familial pancreatic cancers, high-grade prostate cancer and other tumors exhibiting genetic defects in DNA repair genes.
- Discovery of novel “DNA repair enhancing” drugs that may lead to strategies for cancer prevention in **BRCA1** mutation carriers.
- Commitment to using advances in next-generation DNA sequencing to identify novel risk alleles and risk modifying variants in the germline of individuals and families with elevated cancer risk profiles. The Program has initiated numerous projects to sequence DNA, including whole genomes, from potentially informative families, as well as cohorts of patients to better define risk estimates based on identified SNPs.
- Application of genomics to tumor biology to provide a personalized approach to targeted therapeutics by profiling molecular alterations in metastatic, advanced cancers.
- A Molecular Tumor Board to provide consultation and expert opinion on tumor genomic findings, including those that may have a hereditary basis and familial implications for cancer risk.

### CANCER GENETICS PROGRAM FEATURES

The Program sees nearly 2000 new patients each year. Many Program patients have a family history of cancer, including breast, ovarian, colorectal, gastric, pancreatic, endometrial, and others. More than half the patients are considered for genetic testing for Breast/Ovarian Cancer Syndrome (**BRCA1** and **BRCA2** genes) or Lynch Syndrome (hereditary colorectal cancer caused by mutations in DNA mismatch repair genes).

### GENETIC COUNSELING AND TESTING SERVICES FOR THOSE WITH RISK OF INHERITED CANCER INCLUDE

- **Risk Assessment.** Encompasses a complete personal and family medical history, including risk for cancer as well as possible predisposition for carrying a cancer gene. In individuals with a strong family cancer history, a major inherited cancer predisposition gene may be responsible. The characteristics of genetic cancers include:
  - 1) diagnosis at an early age,
  - 2) bilateral or multiple tumors, and
  - 3) multiple generations affected on the same side of the family.
- **Genetic Counseling.** Trained genetic counselors provide:
  - Education regarding cancer susceptibility, risk assessment, and genetic testing.

- Non-directive assistance with decision making.
- Support in identifying and coping with the psychological and social concerns related to an increased cancer risk.
- Discussion of the familial implications of hereditary cancers.
- **Genetic Testing and Results.** If genetic testing is pursued, a second session will be scheduled to discuss results and plan management strategies. Genetic risks for other family members can be reassessed. Interpretation of genetic variants of unknown significance is provided.
- **Risk Reduction.** Depending on personal and family medical history, the type of cancer in question and any applicable genetic test results, the clinic's genetic oncology specialists offer options and recommendations for surveillance, preventative treatments, screening tests, and procedures. These may include intensive monitoring, medications, or surgery. If appropriate, participation in research protocols and clinical trials will be offered.
- **Psychological Support.** Genetic cancer risks pose complex personal and family issues. Coping with the diagnosis of cancer or the potential risk of cancer is a major psychological challenge. With this in mind, the clinic staff may arrange referrals to professional counseling services and support groups.

## CURRENT STUDIES INCLUDE

### Multiple/Variety

- Tumor Genomic Profiling: A Personalized Medicine Approach (VAR0114)
- My Pathway: An Open-Label Phase IIA Study Evaluating Trastuzumab/Pertuzumab, Erlotinib, Vemurafenib/ Cobimetinib, and Vismodegib in Patients Who Have Advanced Solid Tumors with Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents (VAR0115)
- Molecular Analysis for Therapy Choice (MATCH) (ECOG-ACRIN-EAY131)

### Breast Cancer

- Measuring Real-World Breast Cancer Outcomes: The Oncoshare Project

- Developing a Decision Tool for Women with **BRCA 1/2** Mutations

- Treatments and Outcomes of Women with **BRCA1/2** Variants of Uncertain Significance

- Genetic & Pathological Studies of **BRCA1/ BRCA2:** Associated Tumors & Blood Samples (BRSNSTU0020)

- A Phase II Clinical Trial of the PARP Inhibitor Talazoparib in BRCA1 and BRCA2 Wild-Type Patients with (i) Advanced Triple-Negative Breast Cancer and Homologous Recombination Deficiency, and (ii) Advanced HER2-Negative Breast Cancer or Other Solid Tumors with Either a Mutation in Homologous Recombination Pathway Genes (BRS0050)

- The Comparative Effectiveness of Emerging Diagnostic Technologies in Breast Cancer Care

### Gastrointestinal Cancer

- Molecular Genetic and Pathological Studies of Colorectal Tumors and Blood Samples (COR0005)

- Clinical & Pathological Studies of Upper Gastrointestinal Carcinoma (GIUPR0001)

### Gynecologic Cancer

- Prospective Collection of Samples to Enable the Validation of Circulating DNA Biomarkers for the Early Detection of Ovarian Cancer (GYNOVA0034)

### Pancreatic Cancer

- A Phase III, 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)

### Other

- USC Norris Comprehensive Cancer Center and Stanford Cancer Institute Cancer Genetics Hereditary Cancer Panel Testing
- Genetic Studies of Blood and Tumor Samples from Patients with High Inherited Cancer Risk
- Stanford Cancer Genetics Database Study

• *highlighted studies are Stanford investigator initiated*

# Developmental Therapeutics

Phase 1 and 2 Clinical Research Program for Multiple Cancers



Stanford Cancer Center's Developmental Therapeutics (DT) Program, led by director Shivaani Kummar, MD, offers Phase 1 and 2 clinical trials designed to evaluate new treatments 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. Her research interests focus on developing novel therapies for cancer. Dr. Kummar 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. Dr. Kummar has published numerous articles in medical journals and serves on a number of national and international scientific committees. We are excited to have Dr. Nam Bui join Dr. Kummar's team in August 2017. Dr. Bui earned an undergraduate degree in

computer science at Stanford University and went on to earn his medical degree from the University of Texas Southwestern Medical Center. He completed internal medicine residency at Stanford Hospital and thereafter a fellowship in hematology & oncology at the University of California San Diego (UCSD). While at UCSD, he performed extensive research in bioinformatics and tumor genetic sequencing. He joins Stanford Cancer Institute as an oncologist in the Developmental Therapeutics and Sarcoma programs.

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 1 and 2 studies.

## PHASE 1 AND 2 STUDIES

### Multiple Solid Tumor Sites

- An Open-label Phase I Dose-escalation Study to Evaluate the Safety, Tolerability, Maximum Tolerated Dose, Pharmacokinetics, and Pharmacodynamics of the Anti-C4.4a Antibody Drug Conjugate BAY 1129980 in Subjects with Advanced Solid Tumors Known to Express C4.4a (VAR0146)
- Phase 1/2 Multicenter Trial of ICOS Agonist Monoclonal Antibody (mAb) JTX-2011 Alone or in Combination with Nivolumab in Adult Subjects with Advanced Refractory Solid Tumor Malignancies (VAR0143)
- A Phase 1/1b, Open-Label, Multicenter, Repeat-Dose, Dose-Selection Study of CPI-444 as Single Agent and in Combination with Atezolizumab in Patients with Selected Incurable Cancers (VAR0141)
- A Phase 1b/2, 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)
- Phase 1/2, First-in-Human, Dose-Escalation Study of X-396 in Patients with Advanced Solid Tumors and Expansion Phase in Patients with ALK+ Non-Small Cell Lung Cancer (VAR0098)
- A Phase 2 Basket Study of the Oral TRK Inhibitor LOXO-101 in Subjects with NTRK Fusion-Positive Tumors (VAR0136)
- NCI 9938: Phase I Clinical Trial of VX-970 in Combination with the Topoisomerase I Inhibitor Irinotecan in Patients with Advanced Solid Tumors (VAR0144)
- A Phase I, First-in-Human, Open Label, Dose Escalation Study of MGD009, A Humanized B7-H3 x CD3 Dual-Affinity Re-Targeting (DART®) Protein in Patients with Unresectable or Metastatic B7-H3-Expressing Neoplasms and Neoplasms Whose Vasculature Expresses B7-H3 (VAR0148)
- A Phase 1/2a Study to Assess the Safety, Pharmacokinetics, and Pharmacodynamics of PLX8394 in Patients with Advanced, Unresectable Solid Tumors (VAR0129)
- A Phase 1, Open-Label, Dose-Escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Antitumor Activity of ADCT-502 in Patients with Advanced Solid Tumors with HER2 Expression (VAR0150)
- A Phase III Study of AL3818 (Anlotinib) Hydrochloride Monotherapy in Subjects with Metastatic or Advanced Alveolar Soft Part Sarcoma, Leiomyosarcoma and Synovial Sarcoma (SARCOMA0026)
- A Phase 1/2 Study to Investigate the Safety, Pharmacokinetics and Efficacy of ED0-S101, a First-In-Class Alkylating Histone Deacetylase Inhibition (HDACi) Fusion Molecule, In Patients with Advanced Solid Tumors (VAR0152)
- A Phase 1/2 Study of the TRK Inhibitor LOXO-195 in Adult Subjects with NTRK Fusion (Previously Treated) or Non-Fusion NTRK Altered Cancers (VAR0154)

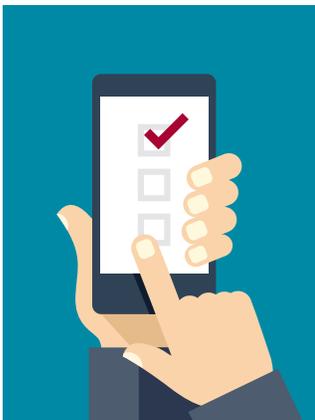
### Opening Soon: November 2017

- A First-in-Human Phase 1, Dose Escalation, Safety and Pharmacokinetic Study of PF-06647020 in Adult Patients with Advanced Solid Tumors (VAR0130)

**Stanford Health Care**  
300 Pasteur Drive, MC 5547  
Stanford, CA 94305

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