Welcome to the Winter 2014 issue of the Stanford Cancer Institute 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 clinical trials and programs available at the Stanford Cancer Institute.

We have more than 300 cancer clinical trials open. We offer highly innovative therapeutic options including trials that are designed by our own Stanford cancer physicians and are only available here. Many of these trials provide access to novel therapies including new “targeted” agents, and often are not available in the community.

As the Director of the Division of Gynecologic Oncology and the Gynecologic Oncology Care Program at Stanford, I am pleased to introduce our multi-disciplinary program in Women’s Cancers. Our physicians and nurses at the Stanford Women’s Cancer Center take great pride in providing excellent care to women with breast and gynecologic cancers, including ovarian, uterine, and cervical cancer. We offer many supportive services including social services, psychological counseling, nutritional counseling, sexual health, palliative care, and integrative medicine.

We have a wide spectrum of treatment options available to our patients, including advanced surgical techniques like robotic surgery, and innovative clinical trials such as immunotherapy and unique radiation techniques. Our Breast Oncology Program is a national leader in targeted therapy for breast cancer.

The Urologic Oncology Program features cutting-edge clinical studies and treatment expertise for complex cancers of the prostate, kidney, bladder, and testis. Care is tightly integrated through joint clinics 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.

Each of the three profiled disease programs offers weekly, multi-disciplinary Tumor Board meetings that serve as a forum for the presentation of challenging cancer cases. During these meetings, treatment options are discussed with all relevant subspecialists.

Stanford’s Clinical Cancer Genetics Program is committed to detecting familial risk for cancer before the disease is diagnosed and becomes difficult to treat. The Program concentrates on clinical and translational research of inherited cancer syndromes, genetic counseling and testing, and cancer risk assessment and reduction for patients with hereditary cancer syndromes.

We hope that you will consider Stanford Cancer Institute for your patients who might be appropriate for clinical trials, multi-disciplinary consultation, or genetic testing for inherited cancers. 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.

Oliver Dorigo, MD, PhD
Director and Associate Professor, Division Gynecologic Oncology
Stanford Women’s Cancer Center
As part of the Stanford Women’s Cancer Center, the Stanford Breast Oncology Program provides an array of innovative studies and treatment by a team of researchers and specialists whose expertise spans all breast cancer related disciplines and who test new treatments not yet available at other facilities. The Program conducts studies on a wide variety of promising new agents and procedures. Advanced imaging techniques, accelerated partial breast irradiation (APBI) including intra-operative radiation therapy (IORT), and 3D conformal radiation therapy are available.

The Stanford Breast Oncology Program is a national leader in the evaluation of targeted therapy of triple negative breast cancer, and is led by Director Mark Pegram, MD, Professor of Medicine (Oncology), renowned breast cancer research scholar and clinician, translational medicine leader, and Co-Leader of Molecular Therapeutics Program with Dr. Amato Giaccia. In addition, Frederick Dirbas, MD, Associate Professor of Surgery (General Surgery), is Co-Leader, Breast Cancer Clinical Research Group, and Physician Leader, Breast Cancer Clinical Care Program. Another renowned breast oncologist who sees patients as a part of this program is George Sledge, MD, Division Chief, Medical Oncology, and Professor of Medicine (Oncology).

STANFORD BREAST ONCOLOGY
RESEARCH BREAKTHROUGHS

• DNA microarray technology enabled Stanford Cancer Center investigators to use miniscule quantities of tumor tissue to classify breast cancers on a genetic basis. Stanford scientists are developing genomic signatures to better classify tumors as low or high risk and thus more accurately match patients to the right treatment.

• The MagSweeper, an automated device developed at Stanford, isolates and purifies cancer cells from blood with higher capture rates and purity than had been previously possible with commercial technology. Used to study the genetic profiles of circulating cancer cells, this invention is the result of the collaboration of Stanford physicians and basic scientists.

• Cancer stem cell research analyzes and will ultimately target cancer stem cells. Working with breast cancer stem cells, Stanford scientists have found 186 genes that, together, predict the risk of recurrence in breast cancer patients.

• Evaluation of improved visualization techniques for finding cancers in dense breast tissue, including ultrasound elastography.
• National leader in evaluation of targeted therapy of triple negative breast cancer.

HIGHLIGHTS OF THE BREAST ONCOLOGY PROGRAM
• A multi-disciplinary tumor board that includes medical, radiation, and surgical oncologists, as well as dedicated breast radiologists, pathologists, cancer geneticists, nurses, social workers, and psychologists. This weekly tumor board of experts provides a thorough and collaborative review of patient records, radiographs, and pathology results, and discusses recommendations with the patient and family members on site.
• Advanced imaging capabilities, including non-contrast MRI.
• Accelerated, partial breast irradiation (APBI) including intra-operative radiation therapy (IORT) and 3D conformal radiation therapy.
• Poly (ADP-ribose) polymerase (PARP) inhibitors and immunotherapies.
• Breast reconstruction with innovative techniques, including transverse rectus abdominis myocutaneous (TRAM), deep inferior epigastric perforators (DIEP), and other specialized free-flaps that offer an alternative to patients who want options beyond implants.
• A wide array of supportive services, including help in overcoming sexual side effects and changes in body image; and collaborative programs with the Stanford Center for Integrative Medicine that explore the mind-body connection, combining complimentary treatments such as meditation and acupuncture with traditional medical treatments.

CURRENT STUDIES INCLUDE:
Neoadjuvant Therapy
• Vitamin D and Breast Cancer: Does Weight Make a Difference? (BRSADJ0024)
• A Phase I Pharmacokinetic and Randomized Phase II Trial of Neoadjuvant Treatment with Anastrozole plus AZD0530 in Postmenopausal Patients with Hormone Receptor Positive Breast Cancer (BRSADJ0025)
• A Phase II, Multi-Center, Open-Label, Neoadjuvant, Randomized Study of Weekly Paclitaxel with or without LCL161 in Patients with Triple Negative Breast Cancer (BRSADJ0026)

Adjuvant Therapy
• A Phase III Clinical Trial Comparing Trastuzumab Given Concurrently with Radiation Therapy and Radiation Therapy Alone for Women with HER2-Positive Ductal Carcinoma In Situ Resected by Lumpectomy (NSABPB43)
• A Randomized Phase III Trial of Adjuvant Therapy Comparing Chemotherapy Alone (Six Cycles of Docetaxel Plus Cyclophosphamide or Four Cycles of Doxorubicin Plus Cyclophosphamide Followed by Weekly Paclitaxel) to Chemotherapy Plus Trastuzumab in Women with Node-Positive or High-Risk Node-Negative HER2-Low Invasive Breast Cancer (NSABPB47)

*highlighted studies are Stanford investigator initiated*
Breast Oncology Program continued

- Randomized, Multicenter, Open-Label Phase III Study to Evaluate the Efficacy and Safety of Trastuzumab Emtansine Versus Trastuzumab as Adjuvant Therapy for Patients with HER2-positive Primary Breast Cancer Who have Residual Tumor Present Pathologically in the Breast or Axillary Lymph Nodes Following Preoperative Therapy (NSABPB50)

Metastatic
- A Single Arm, Open-Label, Phase 2 Study of MGAH22 (Fc-optimized Chimeric Anti-HER2 Monoclonal Antibody) in Patients with Relapsed or Refractory Advanced Breast Cancer Whose Tumors Express HER2 at the 2+ Level by Immunohistochemistry and Lack Evidence of HER2 Gene Amplification by FISH (BRS0024)
- A Randomized, Phase 2 Study of the Efficacy and Tolerability of Veliparib (a PARP inhibitor) in Combination with Temozolomide or Veliparib in Combination with Carboplatin and Paclitaxel versus Placebo Plus Carboplatin and Paclitaxel in Subjects with BRCA1 or BRCA2 Mutation and Metastatic Breast Cancer (BRSMTS0017)
- An Open-Label, Multicenter Extension of Trastuzumab-MCC-DM1 (T-DM1) Administered as a Single Agent or in Combination with Other Anti-Cancer Therapies in Patients Previously Treated with the Equivalent T-DM1 Regimen in a Genentech and/or F. Hoffmann-La Roche LTD. Sponsored T-DM1 Study (BRSMTS0020-EXT)
- Randomized, Double-Blind, Placebo-Controlled Phase II Trial of Fulvestrant (Faslodex) plus Everolimus in Post-Menopausal Patients with Hormone-Receptor Positive Metastatic Breast Cancer Resistant to Aromatase Inhibitor Therapy (ECOGPRE0102)
- A Randomized Phase III Trial of the Value of Early Local Therapy for the Intact Primary Tumor in Patients with Metastatic Breast Cancer (ECOGE2108)

Surgery
- Impact of Breast Conservation Surgery on Surgical Outcomes and Cosmesis in Patients with Multiple Ipsilateral Breast Cancers (MIBC) (ACOSOGZ11102)
- A Randomized Phase III Trial of the Value of Early Local Therapy for the Intact Primary Tumor in Patients with Metastatic Breast Cancer (ECOGE2108)

Radiation Oncology
- Phase II Study to Investigate Concurrent Lapatinib and Radiotherapy in Locally Advanced or Locally Recurrent Breast Cancer and the Impact on Breast Cancer Stem Cells (BRS0027)
- A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chestwall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients with Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy (RTOG1304-NSABPB51)

Imaging Protocols
- The Role of SPY Elite® Intra-Operative Angiography in Determining Adequate Skin Perfusion in Breast Cancer Related Procedures (BRS0005)
- Magnetic Resonance Imaging of Breast Cancer (BRSNSTU0004)
- A Pilot Study to Assess the Utility of Indocyanine Green™ (IC-GREEN™) SPY Elite Imaging in the Mapping of Arm Draining Lymphatics and Nodes during Sentinel Node Resection with or without Axillary Dissection in Breast Cancer (BRS0022)
- Imaging and Blood Biomarkers in Benign and Malignant Breast Disease (BRS0023)

Biomarker & Molecular
- Immunohistochemical & Immunoblot Analysis of NIS (Na+/I-Symporter in Archival and Frozen Human Tissue Samples) (BRSNSTU0011)
The Stanford Gynecologic Oncology Program, which is 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.

To accomplish this mission within the next few years, Dr. Dorigo and his colleagues are applying a multifaceted strategy. Their immediate plan is to rapidly expand Stanford Medical Center’s clinical services and to further develop the existing clinical and scientific activities. In addition, Dr. Amer Karam, MD, was recently appointed as the Director of Outreach and Robotic Surgery in Gynecologic Oncology at Stanford Hospital & Clinics, and as Associate Chief of the Division of Gynecologic Oncology.

Dr. Karam received his medical education from the American University of Beirut Medical School. He completed his residency at the Johns Hopkins School of Medicine and his fellowships at the University of California, Los Angeles, Cedars-Sinai Medical Center and the Memorial Sloan-Kettering Cancer Center. Dr. Karam has extensive experience with cutting edge robotic and minimally invasive surgery. He is currently working on further expanding the Gynecologic Oncology Program at outreach sites in Los Gatos and Turlock.

The Program is led by Jonathan Berek, MD, MMS, Director of the Stanford Women’s Cancer Center, Chair of the Stanford Department of Obstetrics and Gynecology, and the Laurie Kraus Lacob Professor at Stanford School of Medicine; and, Oliver Dorigo, MD, PhD, Associate Professor of Obstetrics and Gynecology, and Director of the Gynecologic Oncology Division and the Stanford GYNECOLOGIC ONCOLOGY CLINICAL CARE PROGRAM

The mission of the Division of Gynecologic Oncology in partnership with Stanford Hospital and Clinics is to provide the most excellent and comprehensive care for women with gynecologic cancer. The Program is committed to the development of novel therapeutic and diagnostic strategies that will improve the prognosis and quality of life for Stanford patients. 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.

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 Laurie Kraus Lacob Program for Gynecologic Oncology and Ovarian Cancer Research and Treatment, and the Cooperative
Ovarian Cancer Group (COGi). Based at Stanford, the Cooperative Ovarian Cancer Group (COGi), a national cooperative research group for specialized treatments in ovarian cancer, offers novel drugs, vaccines, and immunotherapies to patients treated in the Gynecologic Oncology Program. The goal is to improve outcomes for this challenging disease.

RESEARCH PROGRAMS INCLUDE:

• Isolation of ovarian cancer stem cells and the development of stem-cell directed immunotherapy using monoclonal antibodies.

• Understanding the role of the immune system in ovarian cancer to better develop novel therapies.

• Development of vaccines derived from tumor-associated antigens to prevent disease relapse, using a cell-base therapy with genetically-programmed dendritic cells.

• 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.

• Investigation of the mechanisms of HPV-induced malignancy and innovative prevention and detection strategies related to cervical cancer.

SPECIAL CLINICAL PROGRAMS

Multi-disciplinary Tumor Board. The Stanford Gynecologic Tumor Board includes gynecologic oncologists, radiologists, pathologists, nuclear medicine specialists, and nurse 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.
  — Optimal cancer surgery involving the use of state-of-the-art techniques.
  — Advanced robotic surgery and other minimally invasive surgical techniques.
  — Use of leading-edge experimental treatments, including PARP inhibitors, anti-angiogenic therapies, and immunotherapies such as dendritic cell therapy and vaccines against ovarian cancer.
  — 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 that have completed their treatment including surgery, radiation and chemotherapy.
CURRENT STUDIES INCLUDE:

Ovarian/Peritoneal/Fallopian

- GOG 213 A Phase III Randomized Controlled Clinical Trial of Carboplatin and Paclitaxel Alone or in Combination or with Bevacizumab followed by Bevacizumab and Secondary Cytoreductive Surgery in Platinum-Sensitive, Recurrent Ovarian, Peritoneal Primary and Fallopian Tube Cancer (First recurrence) (GOG0213)
- GOG 273 Chemotherapy Toxicity in Elderly Women with Ovarian, Peritoneal or Fallopian Tube cancers (GOG0273)
- Endocyte – A Phase 3 Randomized, Double Blind Trial Comparing EC 145 and Pegylated Liposomal Doxorubicin in Combination Versus PLD in Participants with Platinum-Resistant Ovarian Cancer (GYNOVA0017)
- Prima BioMed-CANVAS: A Randomized, Double Blinded, Placebo-Controlled Trial of CVac (Autologous Dendritic Cells Pulsed with Recombinant Human Fusion Protein) as Maintenance Treatment in Patients with Epithelial Ovarian Cancer in Complete Remission Following First Line Chemotherapy (GYNOVA0023)
- Quest PharmaTech, Inc-Phase 2 Randomized Controlled Study on the Effectiveness of First Line Chemotherapy (Carboplatin-Paclitaxel) versus Chemo-immunotherapy (Carboplatin-Paclitaxel-Oregovamab) in Patients with Advanced Epithelial Ovarian, Adenxal or Peritoneal Carcinoma (GYNOPF0009)
- Does Palliative Chemotherapy Improve Symptoms in Women with Recurrent Ovarian Cancer? (Quality Of Life Study) (GYNOVA0026)
- Tesaro - Phase 3 Randomized Double-Blind Trial of Maintenance with Niraparib Versus Placebo in Patients with Platinum Sensitive Ovarian Cancer (GYNOVA0029)

• Merck - Phase 2 Randomized Study Evaluating MK-1775 in Combination with Paclitaxel and Carboplatin Versus Paclitaxel and Carboplatin Alone in Adult Patients with Platinum Sensitive p53 Mutant Ovarian Cancer (GYNOVA0025)
• Array Biopharma Inc. - Phase 3 The MILO (MEK Inhibitor in Low-Grade Serous Ovarian Cancer): A Multinational, Randomized, Open-label Study of MEK162 Versus Physician’s Choice Chemotherapy in Patients with Recurrent or Persistent Low-grade Serous Carcinomas of the Ovary, Fallopian Tube or Primary Peritoneum (GYNOPF0010) SOON TO OPEN
• Merck - Phase 2 Randomized Study Evaluating MK-1775 in Combination with Paclitaxel and Carboplatin Versus Paclitaxel and Carboplatin Alone in Adult Patients with Platinum Sensitive p53 Mutant Ovarian Cancer (GYNOVA0025)
• Array Biopharma Inc. - Phase 3 The MILO (MEK Inhibitor in Low-Grade Serous Ovarian Cancer): A Multinational, Randomized, Open-label Study of MEK162 Versus Physician’s Choice Chemotherapy in Patients with Recurrent or Persistent Low-grade Serous Carcinomas of the Ovary, Fallopian Tube or Primary Peritoneum (GYNOPF0010) SOON TO OPEN
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 of Urology, Stanford University Medical Center, and Sandy Srinivas, MD, Associate 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 significant other 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.

- 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 and high dose interleukin-2 for advanced renal cell carcinoma.
- 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.

**CURRENT STUDIES INCLUDE:**

**Bladder**

- Open vs. Robotic-Assisted Radical Cystectomy: A Randomized Trial (BLDR0002)
- A Phase II Study of Pazopanib in Combination with Weekly Paclitaxel in Refractory Urothelial Cancer (BLDR0010)

*highlighted studies are Stanford investigator initiated*
• A Randomized, Phase 2, Open-Label Study Evaluating DN24-02 as Adjuvant Therapy in Subjects with High Risk HER2+ Urothelial Carcinoma (BLDR0013)

• Optical Imaging of Bladder Cancer with Molecular Contrast Agents (BLDR0014)

• Evaluation of the Xpert® Bladder Assay For Monitoring of Recurrence in Bladder Cancer Patients and Detection of Bladder Cancer in Symptomatic Patients (BLDR0015)

• A Randomized Doubled-Blinded Phase III Study Comparing Gemcitabine, Cisplatin, and Bevacizumab to Gemcitabine, Cisplatin, and Placebo in Patients with Advanced Transitional Cell Carcinoma (ECOGC90601)

• A Phase III Surgical Trial to Evaluate the Benefit of a Standard versus an Extended Pelvic Lymphadenectomy Performed at Time of Radical Cystectomy for Muscle Invasive Urothelial Cancer (ECOGS1011)

Kidney

• A Randomized, Open-Label, Phase 3 Study of BMS-936558 vs. Everolimus in Subjects with Advanced or Metastatic Clear-Cell Renal Cell Carcinoma Who Have Received Prior Anti-Angiogenic Therapy (RENALE0025)

• Pilot Study of Local Tumor Irradiation with Autologous T-Cell Infusion for Metastatic Renal Cell Carcinoma (RENALE0027)

• A Randomized Phase II Trial of Sunitinib/Gemcitabine or Sunitinib in Advanced Renal Cell Carcinoma with Sarcomatoid Features (ECOGE1808)

• Parallel (Randomized) Phase II Evaluation of ARQ 197 and ARQ 197 in Combination with Erlotinib in Papillary Renal Cell Carcinoma (ECOGS1107)

Prostate

• Quality of Life Following Radical Prostatectomy (PROS0012)

• Canary Prostate Active Surveillance Study Protocol (PROS0026)

• Transrectal Photoacoustic Imaging of the Prostate (PROS0044)

• A Phase 3, Randomized, Double-Blind, Controlled Trial of Cabozantinib (XL184) vs. Mitoxantrone Plus Prednisone in Men with Previously Treated Symptomatic Castration-Resistant Prostate Cancer (PROS0048)

• A Randomized, Double-blind, Phase 3 Efficacy Trial of PROSTVAC-V/F ± GM-CSF in Men with Asymptomatic or Minimally Symptomatic Metastatic, Castrate-Resistant Prostate Cancer (PROS0050)

• STRIVE: A Multicenter Phase 2, Randomized, Double-Blind, Efficacy and Safety Study of Enzalutamide vs. Bicalutamide in Men with Prostate Cancer who have Failed Primary Androgen Deprivation Therapy (PROS0052)

• A Study of HSP90 Inhibitor AT13387 Alone or in Combination with Abiraterone Acetate in the Treatment of Castration-Resistant Prostate Cancer (CRPC) no Longer Responding to Abiraterone (PROS0053)

• A Phase 2 Study of Recombinant Glycosylated Human Interleukin-7 (CYT107) After Completion of Standard FDA Approved Therapy With Sipuleucel-T (Provenge®) for Patients With Asymptomatic or Minimally Symptomatic Metastatic Castration-Resistant Prostate Cancer (mCRPC) (PROS0054) SOON TO OPEN

• Highlighted studies are Stanford investigator initiated
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 familial 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, genetic counseling and testing, and 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, Associate Professor of Medicine and Genetics, in the Division of Oncology. Faculty members include Allison Kurian, MD, MSc, Assistant 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, Associate Professor of Medicine, in the Division of Gastroenterology, who focuses on hereditary GI cancers. Staff includes four full-time certified genetic counselors, a program manager, and a research assistant.

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. Research features:

- Breakthroughs in techniques to sequence multiple genes at a time (multi-gene panels), which is beginning to provide answers for families who test negative for mutations in single, highly penetrant genes such as BRCA1/2 or TP53. This kind of technology, in the past too difficult or expensive, is becoming more readily available and closer in cost to a standard genetic test.
- 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.

- Clinical trials and early adopters of breast MRI for early detection of breast cancer in women at high genetic risk.
- Major research efforts involving the study of individuals and families with hereditary BRCA1/2 mutations. 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.
- 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.)
- 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, and other tumors.
- The first large neoadjuvant trial of defective DNA repair directed chemotherapy in BRCA1/2 carriers with newly diagnosed breast cancer. This study demonstrated a remarkable clinical response rate.
- Use of ovarian tissue for studies of cancer risk and progression. The Program procures these specimens from 40-60 BRCA1/2 mutation carriers per year who undergo risk-reducing bilateral salpingo-oopherectomies (RRSO), and is currently planning a study of chemoprevention in this cohort of women using a PARP inhibitor and measuring tissue changes in these prophylactic ovarian resections.
- Examination of cost-benefit regarding medical outcomes and financial cost to “universal” screening of all resected colorectal and endometrial cancers for Lynch syndrome associated pathological changes (MSI), regardless of family history.
- 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 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.

CANCER GENETICS PROGRAM FEATURES
The Program sees 600 to 700 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.** Specially 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.

- **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. Options 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:

#### 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)
- 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)
- The Gastric Cancer Foundation: A Gastric Cancer Registry (GI0005)
- Clinical & Pathological Studies of Upper Gastrointestinal Carcinoma (GIUPR0001)

#### Other

- Genetic Studies of Blood and Tumor Samples from Patients with High Inherited Cancer Risk
- Molecular Genetic Studies of Childhood Cancer and Blood Samples
- Stanford Cancer Genetics Database Study

*highlighted studies are Stanford investigator initiated*
Stanford Cancer Center’s Developmental Therapeutics Program, led by Branimir I. Sikic, MD, offers Phase 1 and 2 clinical trials using novel therapeutics. Dr. Sikic’s clinical interests are mainly in ovarian cancers and cancers of unknown primary. Other faculty participating in this effort include Drs. Heather Wakelee and Joel Neal (lung cancers), Dimitri Colevas (head and neck cancers), George Fisher and Pamela Kunz (GI cancers), Mark Pegram and Melinda Telli (breast cancers), Sunil Reddy (melanoma), and Ranjana Advani and Holbrook Kohrt (lymphomas).

As a translational clinical studies program, Developmental Therapeutics brings together outstanding physicians with internationally regarded scientists to develop novel therapies and diagnostic modalities that utilize cutting-edge science and technologies. This research focuses on early clinical studies, investigator-initiated trials, the development of analytic approaches to enhancing the discovery of drugs and targets, and the analysis of clinical trials.

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

**PHASE 1 STUDIES**

**Multiple Solid Tumor Sites**
- A Phase I, Open-Label, Dose-Escalation Study of the Safety and Pharmacokinetics of MPDL3280A Administered Intravenously as a Single Agent to Patients with Locally Advanced or Metastatic Solid Tumors (VAR0082)
- A Phase I Study of the Safety, Tolerability, Pharmacokinetics and Immunoregulatory Activity of BMS-663513 (Anti-CD137) in Subjects with Advanced and/or Metastatic Solid Tumors (VAR0071)
- A Phase I/II Study of Intratumoral Injection of Ipilimumab in Combination with Local Radiation in Melanoma, Non-Hodgkin Lymphoma and Colorectal Carcinoma (VAR0090)

**Lymphomas**
- A Phase I Study of PF-05082566 as a Single Agent in Patients with Advanced Cancer, and in Combination with Rituximab in Patients with Non-Hodgkin’s Lymphoma (NHL) (LYMNHL0092)

**PHASE 2 STUDIES**

**Thymic Cancers**
- A Phase 2 Study of Amrubicin in Relapsed or Refractory Thymic Malignancies (THOR0003)

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

**highlighted studies are Stanford investigator initiated**
Squamous Cell: Head & Neck, Non-small Cell Lung, Skin, Cervical, Penile, Anal, and Esophageal Cancers
- A Phase II Study of Oral Rigosertib in Patients with Relapsed or Metastatic, Platinum-resistant, Human Papillomavirus Positive or Negative Squamous Cell Carcinoma (VAR0092)

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- Determining the Utility of Tattooing Axillary Lymph Nodes Undergoing Percutaneous Biopsy for Breast Cancer Staging (BRS0026)