HIPPOCRATIC CANCER RESEARCH FOUNDATION

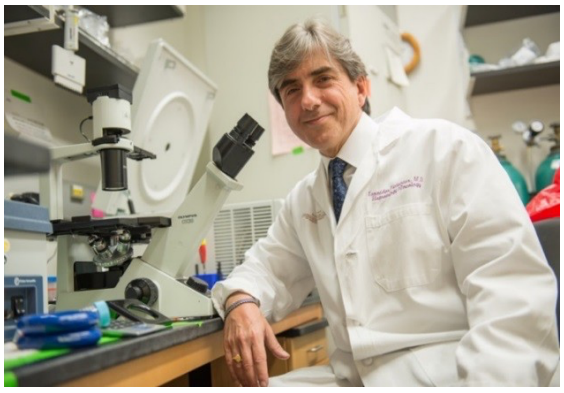
"Wherever the art of medicine is loved, there is also a love for humanity."
~ Hippocrates

Lurie Cancer Center: #1 in Illinois and Top 9 in the Nation

The Hippocratic Cancer Research Foundation (HCRF) supports the research efforts of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. The Lurie Cancer Center has a long-standing history of providing the best in cancer research and patient care. The Lurie Cancer Center is a founding member of the National Comprehensive Cancer Network (NCCN), an alliance of 28 of the world's leading cancer centers dedicated to quality and effectiveness of cancer care. Through the NCCN, important guidelines and standards of cancer care are established and emulated at cancer centers throughout the country. The center is also a founding member of the Big Ten Cancer Research Consortium, a network of academic institutions working together on clinical trials that can truly address the critical medical needs of cancer patients.

Comprised of outstanding clinicians and scientists, the Lurie Cancer Center has approximately 300 researchers who have annually been awarded $200 million in NIH federal funding for cancer-relevant research. Together they bring the knowledge gained through basic, clinical and translational research directly to our patients. The Lurie Cancer Center and our physicians treat nearly 16,000 cancer patients each year, offering a full range of prevention, early detection, treatment, rehabilitation and palliative care programs for all types of cancer. In addition to the excellence of our clinical care, the Lurie Cancer Center has cultivated major research strengths in a variety of areas, including: breast cancer, gynecologic cancers, gastrointestinal and digestive cancers, neurologic cancers, sarcoma, melanoma as well as pediatric cancers. With over 150,000 square feet of space dedicated to research and administrative support, the Lurie Cancer Center provides access to the shared resources of cell imaging, pathology, genomics, clinical research and more.

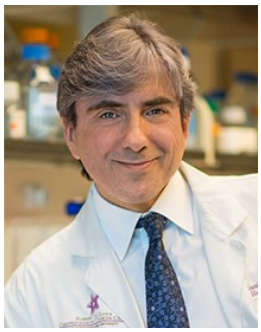
"We are positioned among an elite group of top cancer centers in the country and poised for the next phase of growth," said Leonidas Platanias, MD, PhD, director of the Lurie Cancer Center and member of the Scientific Advisory Board of HCRF *(pictured at right)*. "We look forward to expanding our capabilities and intensifying our efforts to defeat cancer as a disease. We have exciting plans for the future. We are also expanding our precision medicine capabilities and leading-edge clinical trials across the rapidly growing Northwestern Medicine network."



The Hippocratic Cancer Research Foundation's diverse network of donors provides the philanthropic support to fund interdisciplinary cutting edge research teams at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, empowering their world-class investigators to join forces and address the most urgent questions in the fields of cancer biology and oncology in daring and innovative ways. By investing in "out of the box" research, with an emphasis on translational cancer research, the HCRF will accelerate and heighten the impact of scientific discoveries. The proceeding pages provide highlights on the very important investment that has been made in research at the Lurie Cancer Center by the Hippocratic Cancer Research Foundation.

LURIE CANCER CENTER PROGRAMS AND RESEARCH EFFORTS SUPPORTED BY FUNDS RAISED BY THE HIPPOCRATIC CANCER RESEARCH FOUNDATION

Translational research combines clinical observation and laboratory research to produce advances in our understanding and therapies for the treatment of cancer. Bedside to bench, or bench to bedside, has been the key for medicine's greatest successes. HCRF support facilitates crucial laboratory-based efforts that have the potential to lead to important discoveries and a deeper understanding of all cancers. Translational research studies funded by and led by top researchers in the Lurie Cancer Center are summarized below.



Understanding how the immune system works and developing immune therapies for cancer

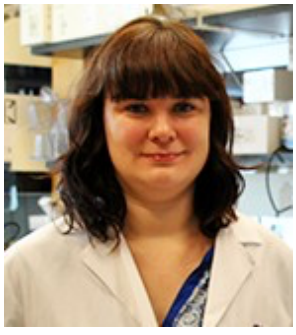
Leonidas C. Platanias MD, Lurie Family Professor of Oncology, Professor of Medicine (Hematology-Oncology) and Biochemistry and Molecular Genetics

The laboratory of Dr. Platanias has been working to understand the role of cytokines called interferons, as mediators of the immune response against cancer cells. With support from HCRF they have shown that some proteins in cancer cells called schlafens can shut down the activation of the immune system in pancreatic cancer cells. This is important, as pancreatic cancer is completely refractory to immune therapy in contrast to other tumors. Dr. Platanias' team is now working with the chemistry core of Northwestern to develop new drugs that can target these proteins. This should result in completely new ways to treat cancer and may apply to different types of tumors. In parallel related work, a clinical trial is currently planned based on the research work that will involve combinations of interferon with a check point immune therapy for pancreatic cancer.

Identifying novel treatment targets in brain tumors

Frank Eckerdt, PhD, Assistant Professor of Neurological Surgery (Research)

Dr. Eckerdt is a key researcher on Dr. Platanias' team and he has been working to identify unique enzymes in brain cancers that can be used to develop novel therapies for glioblastoma, one of the most fatal cancers in humans. With support from HCRF, his work recently established novel pharmacological combinations involving the targeting of special enzymes called MNK kinases. This work is further explored, in collaboration with Dr. Gary Shiltz, a chemist at the Evanston campus of Northwestern, with attempts to develop novel and more specific drugs that block these kinases and, ultimately, can be targeted for the treatment of brain tumors and other cancers.



New agents for the treatment of acute myeloid leukemia

Elspeth Beauchamp, PhD, Assistant Professor of Medicine (Research)

Dr. Beauchamp is has been focusing her work on acute myeloid leukemia, overseing the area of leukemia research in Dr. Platanias' group. She has been working to identify new drugs of an important signaling pathway in malignant cells, called the mTOR pathway. Using a high throughput screening approach with collaborators in the Evanston campus, she has identified a novel drug that blocks a protein that interacts with mTOR, called Sin1. This drug is a unique inhibitor of

mTOR and has activity in the laboratory against leukemia. She is currently working with chemists to optimize the drug to develop it further, ultimately, for clinical use. Beyond leukemia, this drug may have activity against other tumors and will be studied as well.

Immune mechanisms for the treatment of malignant melanoma and other cancers

Diana Saleiro, PhD, Assistant Professor of Medicine (Research)

Dr. Saleiro has been working to understand immune pathways in malignant melanoma, one of the most virulent forms of skin cancer. With the support of HCRF she was able to identify a previously unknown mechanism in melanoma cells, in which interferon pathways and genes correlate with either response or resistance to immune checkpoint inhibitor treatment in melanoma in a context-dependent manner. She has also identified a gene called ULK1, whose expression correlates with survival in melanoma. She is currently examining the role of ULK1 in the generation of immune responses in melanoma and whether combination of inhibitors of ULK1 with immune therapies may provide a new effective approach for the treatment of melanoma.

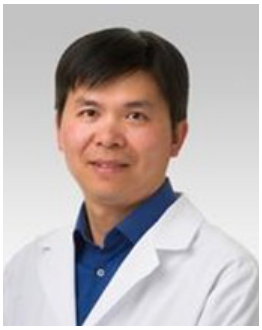
TRANSLATIONAL BRIDGES

A unique, leading-edge initiative, the Translational Bridge Program, supports the creation of interdisciplanary research teams and their ability to join forces, empowering investigators to addresss the most urgent questions in the fields of cancer biology and oncology in daring and innovative ways. This program funds the salary and/or supplies of a research scientist or post-doc working in the laboratory of a translational researcher, who is also supervised by a clinical investigator, aiming to bring the basic research discovery to the clinic.

Novel approach for brain cancer treatment

Roger Stupp, MD Professor of Neurosurgical Surgery, Neurology and Medicine and Craig Horbinski, MD, Professor of Pathology and Neurological Surgery

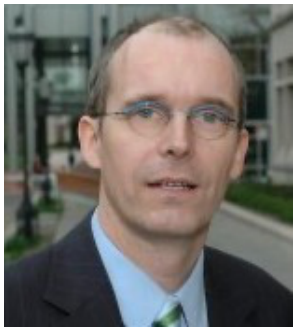
Recipients of a translational bridge award are Roger Stupp, MD, Chief of Neuro-oncology in the Department of Neurology and Professor of Neurological Surgery, Medicine (Hematology and Oncology) and Neurology (Neuro-oncology) (pictured to the left) and Craig M. Horbinski, MD, PhD, Associate Professor of Pathology/ Neurological Surgery (pictured to the right). In an effort to develop novel therapeutics in the treatment of brain tumors, Drs. Horbinski and Stupp have combined efforts to develop an approach to increase the reach of temozolamide to brain tumors. For that purpose they are working to develop an innovative approach involving intracarotid administration to the same side as the tumor. They are using a rat model for GBM patient derived xenograft and so far the results are encouraging, suggesting better activity than oral temozolamide.

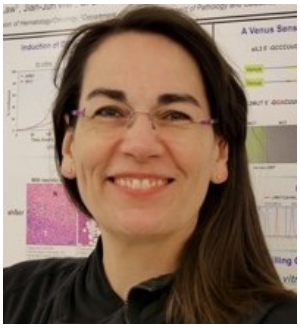


Epigenetic immunotherapy for ovarian cancer

Daniela Matei, MD Professor of Obstetrics &Gynecology and Medicine (Hematology-Oncology) and Bin Zhang, PhD, Professor of Medicine (Hematology-Oncology)

Recipients of a translational bridge award are Daniela Matei, MD, Professor of Obstetrics & Gynecology and Medicine (Hematology and Oncology) (pictured to the left) and Bin Zhang, PhD, Professor of Medicine (Hematology-Oncology) (pictured to the right). This group tries to target the mechanisms by which cancer cells evade immune therapies by modifying their genes. They are developing studies to precisely define how T cells recognize cancer cells and develop approaches to enhance immune tumor targeting. They have made significant advances in defining the mechanisms and plan to use this approach to develop new therapies for ovarian cancer that may impact other cancers as well.





Discovery of a cancer kill code and using it for new cancer treatments

Marcus Peter, PhD Professor of Medicine, Nisha Mohindra, MD, Assistant Professor of Medicine, and Andrea Murmann, PhD, Assistant Professor of Medicine (Research)

Marcus Ernst Peter, PhD, Professor of Medicine (Hematology and Oncology) and Biochemistry and Molecular Genetics (pictured to the left) and Nisha A Mohindra, MD, Assistant Professor of Medicine (Hematology and Oncology) (pictured at the center), and Andrea E Murmann, PhD, Research Assistant Professor of Medicine (Hematology and Oncology) (pictured to the right), combined efforts in their specific research in developing toxic siRNAs and artificial miRNAs for the treatment of cancer, focusing initially on lung cancer. This work is based on the monumental discovery by the Peter group of what they described as the "Huntington's cancer weapon". Identifying this code in cancer cells, they discovered highly toxic siRNAs that can kill all cancer cells in the laboratory, including the human lung cancer cells. Working with a lung cancer doctor - Dr. Nisha Mohindra - they are trying to first develop this treatment for use in lung cancer, one of the most devastating cancers in humans, but the hope is that this treatment will be applied to essentially all different types of cancer. The funds raised by HCRF have facilitated the development of the translational bridge/link between this important laboratory discovery and the clinic.

HIPPOCRATIC SCHOLARS

The Hippocratic Scholar Awards are selected via a thorough review of many applications once a year and each support researchers who have designed highly innovative, cutting-edge basic science that will advance the efforts of Lurie Cancer Center members to eliminate cancer. For this award that provides important research support, the researchers are required to have previously shown evidence of national and international recognition and presence. Three Hippocratic scholars were selected in February 2019.

Hippocratic scholar - John D. Crispino, PhD,
Professor of Medicine (Hematology and Oncology) and Biochemistry and Molecular Genetics

Dr. Crispino is a distinguished researcher, who also serves as Associate Director for Education in the Lurie Cancer Center and serves in the executive committee of the Lurie Cancer Center, chaired by Dr. Platanias. Following in line with Dr. Crispino's interest in molecular genetics, his HCRF funded project is titled "Identifying Chromosome 21 Genes That Protect People with Down syndrome from Solid Tumors: Implications for Cancer Prevention." Research in Dr. Crispino's laboratory is also focused on investigating the regulatory mechanisms governing normal and malignant blood cell development, with an emphasis on understanding the growth of red blood cells and platelet-producing cells. In addition, the group has a major interest in learning how changes in normal essential regulatory molecules lead to human blood diseases, including acute leukemias and myeloproliferative neoplasms (MPNs). The lab seeks to make seminal basic science discoveries while simultaneously translating these discoveries in ways that will benefit patients with hematologic malignancies.

Hippocratic scholar - Arthur B. Prindle, PhD, Assistant Professor of Biochemistry and Molecular Genetics

Dr. Prindle is an exceptional junior researcher, with very high impact national publications, who was recently recruited to Northwestern from University of California, San Diego. Prindle's laboratory is interested in understanding how molecular and cellular interactions give rise to collective behaviors in microbial communities. They use synthetic biology, quantitative microscopy, and microfluidics to directly investigate the molecular mechanisms behind how cells communicate across broad spatial and temporal scales. Their goal is to apply these principles to develop new synthetic biology approaches to biomedical problems through microbiome engineering. Dr. Brindle collaborated with Derek A Wainwright, PhD on the project entitled "Maximizing the Efficacy of Cancer Immunotherapy with an Engineered Microbiome" for which the Hippocratic scholarship was awarded.

Hippocratic scholar - Derek A Wainwright, PhD, Assistant Professor of Neurological Surgery, Medicine (Hematology and Oncology) and Microbiology-Immunology

Dr. Wainwright is an outstanding, NIH funded researcher, with high impact work on the mechanisms by which the immune system attacks cancer, driving efforts to develop new immune approaches for brain tumors and other types of malignancies. He has developed novel tools for his studies, including a humanized immune mouse treatment that makes possible the study of difficult to address immunology-related questions. He was selected to be a Hippocratic scolar for his highly innovative collaboration with Dr. Prindle on maximizing the efficacy of cancer immunotherapy with an engineered microbiome. This approach is emerging as a new immune therapy for cancer by modifiying the natural host bacteria in the gut and it is highly promising as it can be potentially used for all types of cancer.

CANCER CLINICAL TRIALS

Every cancer treatment that is saving lives today is the result of a clinical trial. The Lurie Cancer Center is involved in more than 300 clinical therapy trials at any given time, covering a broad range of research relevant to the 14 cancer-types. The estimated annual cost of clinical trials for the Lurie Cancer Center is $10 million total with philanthropy funding approximately 50 percent of this cost and the remaining cost funded through industry or federal grants.HCRF support has been used to fund highly innovative trials for different types of cancer, reflecting cutting edge research translated to the laboratory. Clinical trials currently being supported in part by HCRF include:

Gynecological Cancers

Physician Lead: Emma Barber, MD
Assistant Professor of Gynecologic Oncology

Study Name: A Pilot, Multicenter, Single Arm, Open Label, Surgical Window of Opportunity Study of Abemaciclib and Letrozole for Endometrioid Adenocarcinoma of the Endometrium

Background: Endometrial cancer is the most common cancer of the female reproductive tract and the fourth most common cancer in the United States. It is estimated that more than 60,000 new endometrial cancer diagnoses will have been made in 2016. For many women, initial therapy is curative.
However, 20-25% of patients with endometrial cancers are initially detected at an advanced stage; these women have a guarded prognosis, poor overall response to chemotherapy and an increased risk of recurrence compared to patients with early-stage disease. In women with advanced endometrial cancer, response rates to the most active single agent chemotherapies range from 20-35%. In the advanced and recurrent setting, chemotherapeutic interventions are limited (NCCN Guidelines Uterine Neoplasms V 1.2015). There is a desperate need to identify additional active therapies for this patient population.

Purpose of the Study: The primary objective is to determine whether there are changes in Ki-67 expression from the pretreatment specimen (e.g. biopsy or D&C) to the post-treatment hysterectomy specimen following treatment with letrozole and abemaciclib.
Secondary Objectives: • To determine the proportion of tumors with complete cell cycle arrest (CCCA) response as measured by Ki-67 expression between the pretreatment tumor and the post-treatment tumor. CCCA response is defined as less than 3% of tumor cells staining positive for Ki-67 from specimens obtained at the time of hysterectomy.
ï To identify biological characteristics of tumors (e.g. MMR status, PTEN mutational status, cyclin D1 expression, etc.) correlating with decreased Ki-67 expression induced by the letrozole and abemaciclib combination.
ï To determine the frequency of adverse events associated with use of abemaciclib and letrozole. Adverse events will be categorized and graded according to CTCAE v5.

Leukemia

Physician Lead: Jessica Altman, MD
Associate Professor of Medicine (Hematology-Oncology)

Study Name: Phase Ib, open label, combination study of nintedanib with 5-azacitidine in newly diagnosed acute myeloid leukemia characterized by HOX gene overexpression, that are not candidates of intensive chemotherapy

Background: Adult acute myeloid leukemia (AML) is a type of cancer in which the bone marrow makes abnormal myeloblasts (a type of white blood cell), red blood cells, or platelets. AML is a life-threatening disease characterized by uncontrolled proliferation of clonal neoplastic hematopoietic precursor cells and impaired production of normal blood cells frequently leading to neutropenia, anemia and thrombocytopenia. If untreated, patients frequently die of infection, bleeding, or complications of leukostasis usually in a matter of weeks. Successive clinical trials have led to a relatively standard induction regimen using an anthracycline and cytarabine followed by repetitive cycles of intensive consolidation chemotherapy, usually with high dose cytarabine. Such treatment is curative for many patients with favorable-risk and some with intermediate-risk cytogenetics, but not suitable for older adults and those with unfavorable-risk cytogenetics. Older adults are both less able to tolerate intensive chemotherapy and the acute leukemia that develop in older adults are frequently more resistant to standard chemotherapy. The median age of diagnosis of AML is between 68 and 72. Outcomes for older adults have been disappointing.

Purpose of the Study: Determination of the Maximum Tolerated Dose (MTD) of nintedanib for combination treatment of nintedanib and 5-azacitidine in the treatment of newly diagnosed and relapsed/refractory acute myeloid leukemia with HOX overexpression and who are ineligible for intensive chemotherapy.

Lymphoma

Physician Lead: Reem Karmali, MD
Associate Professor of Medicine (Hematology-Oncology)

Study Name: Phase I/II Study to Evaluate the Safety and Efficacy of Nivolumab in Combination with R-CHOP in a Cohort of Patients with DLBCL/tFL/ high grade B-NHL

Background: Diffuse large B-cell lymphoma (DLBCL) is an aggressive lymphoma that is predominantly diagnosed in the elderly with prior studies reporting a 30% rate of cases occurring in patients over the age of 70, and increasing in incidence. Although rituximab in combination with cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) is the standard treatment for patients with newly diagnosed DLBCL achieving responses as high as 80-90%, close to 40% of patients will relapse and die of their disease. With the advent of gene expression profiling (GEP) and next-generation deep sequencing, it is now evident that patients with DLBCL possess unique molecular signatures that correspond with their disease phenotype. Gene expression profiling has identified at least 2 distinct subsets of DLBCL with clear phenotypic differences with respect to clinical characteristics and disease course, namely germinal center (GC) versus activated B-cell (ABC). These 2 subsets make up approximately 50% and

30% of DLBCL, respectively, and are associated with differential expression of genes that reflect derivation from different stages of B-cell differentiation and as such, unique oncogenic pathways for pathogenesis.

Purpose of the Study: • Phase I: To identify the maximum tolerated dose (MTD) for the combination treatment of nivolumab and R-CHOP in patients with DLBCL. • Phase II: To look at preliminary efficacy as measured by rate of complete response (CR) for combination nivolumab + R-CHOP • To look at preliminary efficacy as measured by overall response rate (ORR) • To assess the impact of nivolumab + R-CHOP on survival outcomes, specifically, progression free survival (PFS), overall survival (OS) and event-free-survival (EFS) • To assess toxicity and tolerability of nivolumab + R-CHOP • To assess quality of life of nivolumab + R-CHOP Exploratory Objectives: • To explore changes in immune cell subsets and the cytokine/chemokine milieu associated with treatment with nivolumab and evaluate their utility as predictive biomarkers of response • To identify the process of cachexia as a potential mechanism of resistance to anti-PD-1 therapy

Prostate Cancer

Physician Lead: Maha Hussain, MD

Study Name: Clinical, Environmental, Genetic and Genomic Profile of Men with Early-Onset Aggressive Prostate Cancer

Background: Despite advances in therapy, advanced prostate cancer remains a lethal disease; it is the second most common cause of cancer death for men in the United States with an estimated 29,430 deaths expected in 2018 . Local and regional disease carries an excellent 5-year survival of nearly 100% and many older patients are diagnosed with indolent prostate cancer without significant impact on overall survival. As a result, prostate cancer is often considered an "indolent" malignancy that gradually progresses from localized disease to metastatic hormone-sensitive disease (mHSPC), and ultimately metastatic castration-resistant prostate cancer (mCRPC). In reality, prostate cancer is a heterogeneous and diverse disease that includes lethal phenotypes observed in patients with early onset metastatic prostate cancer and patients with progressive disease within a short interval of beginning androgen-deprivation therapy (ADT) ± Docetaxel or abiraterone. The clinical and molecular features of these lethal prostate cancer phenotypes are not well described. The subgroup of high-risk patients with imminently lethal disease is becoming a significant proportion of men diagnosed with prostate cancer. In the decade from 2004-2013 the proportion of patients under the age of 75 years in the SEER database diagnosed with metastatic prostate cancer increased from 2.7% (95% CI 2.5-2.9%) to 4.0% (95% CI 3.8-4.2%). Over the same time period there also was a progressive increase in the portion of patients who were diagnosed with intermediate- and high-grade prostate cancer from 46.3% (95% CI, 45.9-46.9%) to 56.4% (95% CI, 55.9-56.9%). This changing pattern is potentially associated with the change in recommendations for prostate specific antigen (PSA) screening by the United States Preventative Task Force and highlights the increasing importance of understanding clinical and genomic risk factors helpful for identifying patients with potentially lethal disease at diagnosis and understanding its biology.

Purpose of the Study: 1. Characterize the clinical, environmental, genetic and genomic profiles of men presenting with early-onset (age ≤ 60) potentially lethal metastatic prostate cancer (N1 or M1) at diagnosis (cohort 1) or who develop metastases shortly after local therapy (cohort 2) in a multistate, multi-institutional initiative. 2. Characterize the clinical/genomic predictors and mechanisms of early progression on ADT ±

docetaxel or ADT ± abiraterone (≤ 1 year) in men with metastatic hormone sensitive prostate cancer (mHSPC). 3. Develop drug response scores to identify novel agents with potential sensitivity in mHSPC. 4. To prospectively correlate clinical and molecular characteristics with treatment outcomes.

Physician Lead: Alicia Morgans, MD
Associate Professor of Medicine (Hematology-Oncology)

Study Name: Cognitive Effects of Androgen Receptor (AR) Directed Therapies for Advanced Prostate Cancer

Background: Prostate cancer is the most common cancer among American men, and the second leading cause of cancer death in the US. Approximately 40-50% of the nearly 220,000 men diagnosed with prostate cancer each year will receive treatment with androgen deprivation therapy (ADT) at some point during the course of their disease. ADT, accomplished by medical or surgical castration lowering testosterone to <50 ng/dL inhibits signaling through the AR, disrupting tumor progression. It is considered the backbone of treatment of metastatic prostate cancer. Although a majority of men will respond to treatment with ADT, men exposed for long periods of time eventually develop castration-resistant disease with progression of tumor growth despite low levels of testosterone. Perhaps surprisingly, work during the past decade demonstrated that further suppression of AR signaling can provide disease control and prolong life among men with mCRPC.3-6 These novel AR directed therapies accomplish this by impairing testosterone synthesis by the adrenal glands and tumor cells (abiraterone acetate), or by directly antagonizing the AR (enzalutamide). Both are Food and Drug Administration (FDA) approved for treatment across the disease spectrum and neither has demonstrated superiority over the other.

Purpose of the Study: The primary objective is to compare cognitive function of men with advanced prostate cancer during treatment with enzalutamide or abiraterone acetate, adjusted for associated mediators of cognitive function (quality of life, depression, pain, and fatigue). Secondary Objectives: • To identify characteristics of men with advanced prostate cancer associated with change in cognitive function during treatment with AR directed therapy. • To compare quality of life and associated factors, including fatigue, pain, and depression, of men with advanced prostate cancer during treatment with enzalutamide or abiraterone acetate. Exploratory Objectives: • To analyze whether single nucleotide polymorphisms (SNPs) may be associated with change in cognitive function during treatment with AR directed therapy. • To compare the functional and structural components of the brain over time and between the brains of men with advanced prostate cancer treated with enzalutamide or abiraterone acetate using diffusion tensor imaging (DTI), functional MRI (fMRI), arterial spin labeling (ASL), and other advanced neuroimaging techniques.

Breast Cancer

Physician Lead: Massimo Cristofanilli, MD
Professor of Medicine (Hematology-Oncology)

Study Name: I-CURE-1: A Phase II, single arm study of Pembrolizumab combined with carboplatin in patients with circulating tumor cells (CTCs) positive Her-2 negative metastatic breast cancer (MBC)

Background: Circulating tumor cells (CTCs) in Metastatic breast Cancer. Breast cancer mortality has been decreasing considerably over the past two decades as a result of earlier diagnosis and major treatment advances in the adjuvant and metastatic settings. Despite this progress, metastatic disease is still largely considered an incurable condition and 5-year survival rates are less than 25%. Thus, the major treatment objectives in the advanced stage disease remain palliation of symptoms and improvement of quality of life. Importantly, metastatic breast cancer (MBC) is a heterogeneous disease and long-term patient outcome can be influenced by various biological features, as well as by the extent and site of metastatic disease. Typically, widespread visceral disease is associated with symptomatic condition leading to deterioration of the performance status and short survival. Various molecular markers and blood-based tests have been investigated as surrogate for more aggressive disease, among them the most reliable appears enumeration of CTCs. During the last decade, several techniques capable of detecting and quantifying CTCs in cancer patients have been developed. It has been proposed that subpopulation of CTCs with tumor initiating potential act as a central mediator of metastatic dissemination, giving rise to the formation of distant micrometastases, which subsequently generate overt detectable and frequently measurable lesions. In support of this theory, multiple studies have shown that a number of CTCs higher or equal than 5 per 7.5 mL of blood, evaluated before starting systemic treatment, is associated with poor outcome in patients with MBC. In addition, high CTC counts are associated with greater metastatic tumor burden, expressed as number of metastatic sites.

Purpose of the Study: Evaluate the impact on progression-free survival (PFS) with the combination carboplatin - pembrolizumab in patients with CTC positive, HER2 negative MBC previously treated with anthracyclines and taxanes in primary setting; and patients with CTC positive, TNBC, MBC not exposed to other treatments in the metastatic setting.

LOOKING FORWARD

The Hippocratic Cancer Research Foundation has made a major difference in the fight against cancer, by allowing Lurie Cancer Center researchers to develop out of the box ideas for basic science research projects and translational-high impact-clinical trials. The establishment of the Hippocratic Scholar Awards is also a form of recognition for exceptional researchers aiming to develop new treatments for cancer. Going forward, HCRF's support will be even more important for the next phase of research, as the early results can be expanded, translated and lead to new cancer breakthroughs. We are very grateful for HCRF's continued support of the Lurie Cancer Center and we look forward to working jointly with the members of the foundation to accelerate the development of new cures for cancer.

If you have any questions or would like additional information, please do not hesitate to contact:

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