NYU Langone Health

Perlmutter Cancer Center

2019 HIGHLIGHTS

Practice Changing Advance in Bladder Cancer

First FDA approval in 20 years for treatment of non-muscle invasive bladder cancer

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SPORE Grant for Melanoma

Research to focus on developing biomarkers that predict immunotherapy outcomes

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Innovative Genetic Counseling Program

Reshaping strategies around genetic risk assessment for cancer

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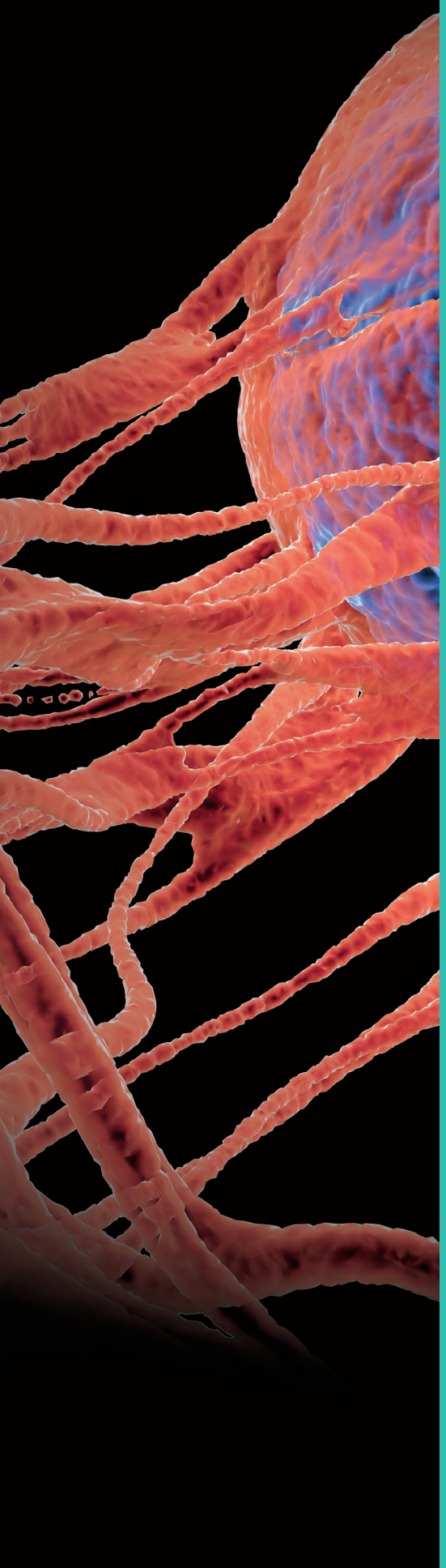
110%
Increase in patient volume over the last five years

NCI-Designated Comprehensive Cancer Center

30
New faculty members over the last three years

73%
Increase in patients enrolled in clinical trials



MESSAGE FROM THE DIRECTOR

BENJAMIN G. NEEL, MD, PHD

Professor of Medicine

Director, Laura and Isaac
Perlmutter Cancer Center

2019 was a banner year for Perlmutter Cancer Center—from research advances to service expansion to Comprehensive Cancer Center designation from the National Cancer Institute (NCI).

We expanded our ability to reach New York City–area patients with the June 2019 opening of a new, multi-specialty outpatient facility offering medical and radiation oncology treatment in Sunset Park, Brooklyn. With this new facility, plus our growing footprint in Long Island, where NYU Langone Health and NYU Winthrop Hospital merged in 2019, we are providing cancer care for more patients than ever, as well as dramatically enlarging our research program.

We also continue to seek new treatment options for the most intractable malignancies. To this end, we have expanded our Phase 1 Drug Development Program, obtained a prestigious SPORE grant for melanoma from the NCI aimed at improving immune therapy, advanced robotic surgery for lung cancer, and led a practice-changing clinical trial for bladder cancer. Meanwhile, advances in genetic screening are helping us to better identify patients at high risk for developing cancer, and intervene earlier to prevent the disease or detect it at an earlier, more curable stage.

We look forward to continuing to build on these areas of strength with the goal of transforming cancer care everywhere, while continuing to provide compassionate, state-of-the-art care to our patients.

Cover image: Computer illustration of cancer cells showing the blood vessel formation providing the cells with oxygens and nutrigens. The cells with their nuclei are shown in blue.

RENDERING: GETTY IMAGES

FDA Approves First Treatment in 20 Years for a Common Type of Bladder Cancer

Pembrolizumab (Keytruda®) was approved in January 2020 by the U.S. Food and Drug Administration (FDA) to treat patients with high-risk, non-muscle invasive bladder cancer (NMIBC) unresponsive to Bacillus Calmette-Guérin (BCG). This is the first second-line treatment for the disease to be approved in the United States since 1998.

PEMBROLIZUMAB FILLS AN UNMET NEED FOR PATIENTS

For patients with BCG–unresponsive high-risk NMIBC, the only curative treatment is radical cystectomy, a surgery with high morbidity and a 4 percent mortality rate. Patients have few available alternative options if they are ineligible for or they elect not to undergo the procedure. Earlier studies showed pembrolizumab, a PD-1 inhibitor, elicited durable antitumor activity in patients with metastatic urothelial carcinoma. The KEYNOTE-057 (NCT02625961) Phase 2 trial was designed to study pembrolizumab's effect on patients with BCG-resistant carcinoma in-situ (CIS) with or without papillary tumors, in which upregulation of the PD-1 pathway has been observed. "High-risk, non-muscle invasive bladder cancer is a serious disease, characterized by frequent recurrences and progression," says Arjun V. Balar, MD, associate professor of Medicine and director of Genitourinary Medical Oncology at NYU Langone Health's Perlmutter Cancer Center. "As a physician who specializes in the management of bladder cancer, it is encouraging to now have a new treatment option for patients whose cancer has become unresponsive to BCG treatment."

KEYNOTE-057 is the first study to demonstrate the effectiveness of a novel systemic immunotherapy for BCG-unresponsive high-risk, non-muscle invasive bladder cancer. The trial showed that pembrolizumab elicited a 41.2 percent complete response rate in patients after the initial four treatments. After a year of treatment, half of those (20 percent) maintained a complete response.

Dr. Balar says that no new safety signals were detected in patients during the trial. For patients whose cancer recurred after treatment with pembrolizumab, the window of opportunity for cystectomy was preserved.

PRACTICE-CHANGING DRUG APPROVALS FOR PATIENTS WITH BLADDER CANCER

Dr. Balar, who was the overall lead principal investigator of the KEYNOTE-057 trial, is among a number of key investigators at Perlmutter Cancer Center who are international leaders in developing more effective, better-tolerated treatments for patients with bladder cancer.

The approval of pembrolizumab for BCG-unresponsive NMIBC is the third practice-changing drug approval Dr. Balar has led in the last three years. In early 2017, the FDA approved atezolizumab (Tecentriq®) and pembrolizumab as first-line treatments for patients with advanced bladder cancer who are too medically frail to take the standard-of-care chemotherapy agent cisplatin. These immune system–boosting agents were the first-ever FDA-approved treatments for cisplatin-ineligible bladder cancer.

In 2019, Gary D. Steinberg, MD, a member of the faculty of urology and director of Perlmutter Cancer Center's Urology Bladder Cancer Program, joined NYU Langone to complement ongoing efforts in the care of patients with bladder cancer. Dr. Steinberg was a scientific advisor for Merck on the KEYNOTE-057 trial and is prinicipal investigator for the KEYNOTE-676 (NCT03711032) Phase 3 study of BCG with or without pembrolizumab for high-risk NMIBC that is persistent or recurrent following BCG induction. Together, Drs. Balar and Steinberg are working to develop the next best treatments for patients with this disease.

"The approval of pembrolizumab is paradigm-changing and offers patients a possible therapy to preserve their native bladder function while eliminating their cancer," says Dr. Steinberg. "This is a breakthrough for some patients and most likely will lead to new combinations of therapy for this aggressive form of localized bladder cancer that will hopefully benefit additional patients. This will lead to further research and innovative treatments for the bladder cancer community and clearly is a significant advance."

"The study demonstrates local activity in the bladder from a systemically administered treatment," Dr. Balar adds. "This is promising since systemic immune activation is what ultimately leads to long-term durable remissions of cancer."

Disclosures: Gary D. Steinberg, MD, is a member of clinical trial protocol committees for Merck, Bristol-Myers Squibb, Janssen, and Cold Genesys. He is a scientific advisor or consultant for Heat Biologics, Cold Genesys, Photocure, Merck, Roche/Genentech, Ciclomed, TARIS Biomedical, MDxHealth, Fidia Farmaceuticals, UroGen Pharma, Ferring Pharmaceuticals, Aduro Biotec, Boston Scientific, Bristol-Myers Squibb, AstraZeneca, Pfizer, Janssen, EpiVax Oncology, Natera, FKD Therapies Oy, EnGene Bio, and Sesen Bio. Dr. Steinberg has equity or stock options in EpiVax Oncology and UroGen Pharma.

Arjun V. Balar, MD, has performed contracted research for Genentech, Merck, AstraZeneca/Medimmune, Nektar, Seattle Genetics and Immunomedics. He has served in a consultant/advisory role for Genentech, Incyte, Janssen, Merck, Pfizer, AstraZeneca/Medimmune, Nektar and Seattle Genetics. He has had speaking engagements with Genentech, Merck and AstraZeneca/Medimmune. He serves on Steering/Scientific Advisory Committees at Merck and Nektar.

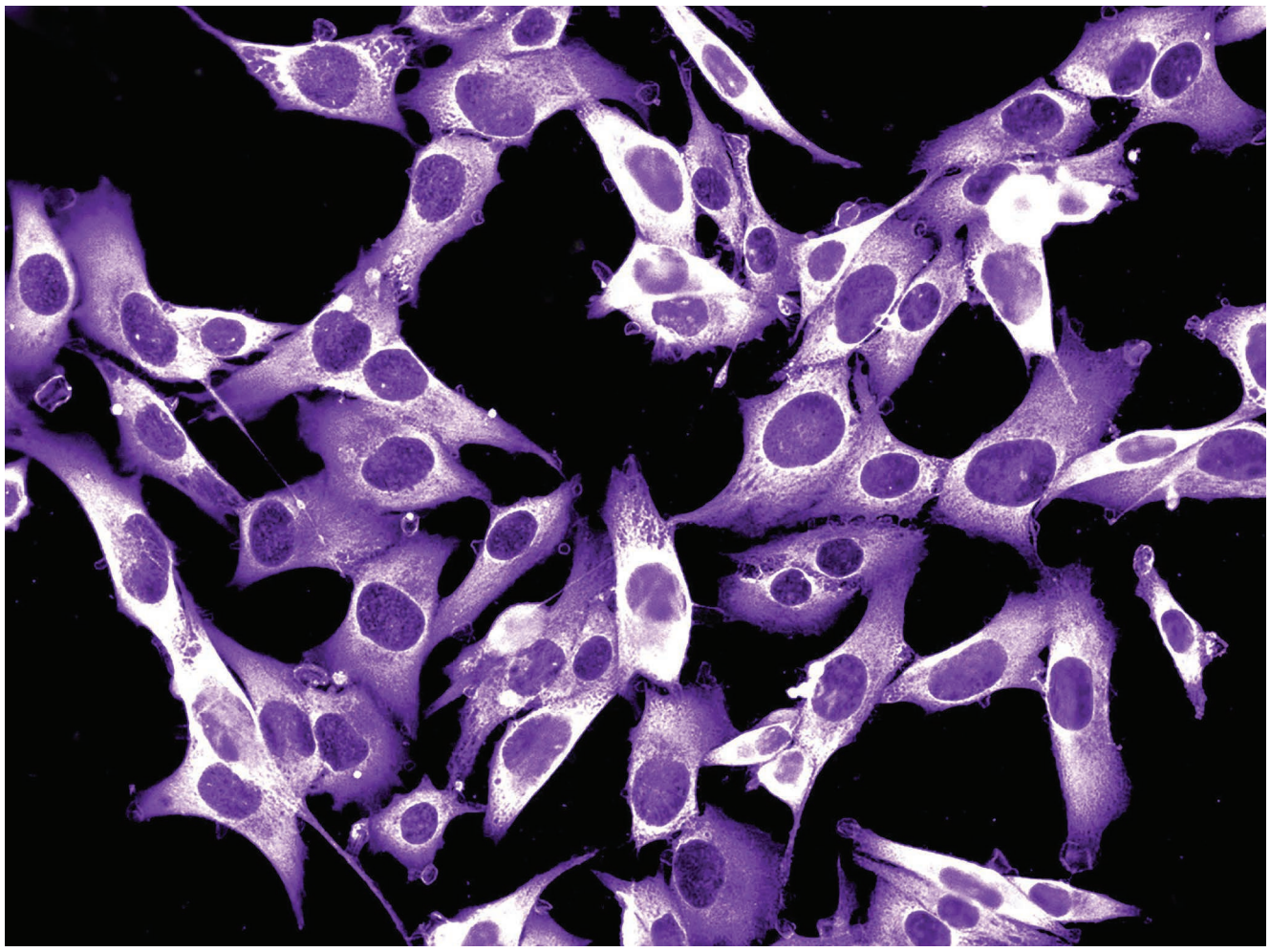
Arjun V. Balar, MD

PHOTO: NYU LANGONE STAFF

In This Article

The grant includes four projects, exploring:

- Role of the microbiome in immunotherapy response
- Predicting relapse-free survival after immunotherapy
- Identifying immunotherapy patients at risk of developing immune-related adverse events such as diarrhea and colitis
- Role of microRNAs in relapse following immuno-therapy in patients with stage II melanoma



NYU Langone physicians and researchers are working to define biomarkers that can predict a patient's response to melanoma treatment and their risk of immune-related side effects.

PHOTO: DLUMEN/GETTY

SPORE Grant Focuses on Developing Biomarkers that Predict Melanoma Immunotherapy Outcomes

The NCI has awarded NYU Langone Health a five-year, $11 million grant to develop better tools to predict which patients with advanced melanoma will benefit from immune checkpoint inhibitors.

URGENT NEED FOR BIOMARKERS

Only 40 to 50 percent of patients successfully respond to immuno-therapy, and a significant percentage experience immune-related toxicity, underscoring the urgent need to define biomarkers to help physicians tailor care. The goal is to predict a patient's response to a treatment and their risk of immune-related side effects.

The SPORE program is investigating "checkpoints"—the sensors on immune cells that cancer cells hijack to turn off immune responses. Checkpoint inhibitors are one type of immunotherapy that counter this effect. But doctors need more detailed guidance on how to use them on surgically treated patients at higher risk of relapse, as well as patients with metastatic disease. Identifying biomarkers that can predict benefit or toxicity is critical and timely, and promises to have broad applicability.

NYU Langone investigators are using a phased approach to develop new biomarkers through four distinct and promising projects. The four projects—each led by a clinician and a basic scientist—span the biomarker development path from target identification and clinical relevance to assay and clinical validation and, ultimately, clinical utility with testing in an investigator-initiated clinical trial.

WORKING TOGETHER FOR A NEW PREDICTION MODEL

Project 1 explores the role of the microbiome in immunotherapy response. It is co-led by Jeffrey S. Weber, MD, PhD, the Laura and Isaac Perlmutter Professor of Oncology in the Department of Medicine and deputy director of Perlmutter Cancer Center, and Jiyoung Ahn, PhD, associate professor in the Departments of Population Health and Environmental Medicine and associate director of population sciences and director of the Epidemiology Program at Perlmutter Cancer Center.

Dr. Ahn, whose research explores how the gut microbiome influences the development of gastrointestinal cancers, proposed a study of stool samples from participants in a randomized Phase 3 adjuvant trial. The trial tests combination PD-1/CTLA-4 blockade versus PD-1 alone in patients with high-risk, resected stage IIIB/C and IV melanoma. The bacteria in the patients' stool samples are analyzed to identify different species that are more likely to be associated with a positive response to immunotherapy or more likely to lead to toxicity.

Dr. Weber is assessing a series of serum and peripheral blood biomarkers whose association with clinical outcome and toxicity will be determined. The goal is to use the combined biomarkers to develop a risk prediction model that can guide physicians' decisions regarding immunotherapy treatment.

HOMING IN ON IMMUNOTHERAPY RESISTANCE

Project 2 aims to identify biomarkers that predict relapse-free survival after immunotherapy. It is co-led by Tomas Kirchhoff, PhD, associate professor of population health and environmental medicine, and Dr. Weber. This project focuses on patients with stage III/IV resected melanoma tumors treated with immunotherapy in the adjuvant setting. It proposes to identify novel T cell–specific transcriptional networks that potentially affect resistance to immune checkpoint inhibitors. The networks may serve as targets for improved adjuvant immunotherapies for melanoma and other cancers.

The team hypothesizes that underlying inherited factors that influence host immunity affect relapse-free survival after adjuvant immunotherapy. The findings from this project could enable clinicians to predict which patients might benefit from immunotherapy.

> *"In my 30-year career, I have seen many attempts to develop treatments for patients with advanced melanoma. It's only recently, with the introduction of immunotherapies, that the landscape of what happens to a patient with advanced melanoma has radically changed."*
>
> **Richard L. Shapiro, MD**

AVOIDING IMMUNE-RELATED TOXICITY

Project 3 addresses a pressing need to identify immunotherapy patients at risk of developing immune-related adverse events such as diarrhea and colitis. It is co-led by Michelle Krogsgaard, PhD, associate professor in the Department of Pathology, and Iman Osman, MD, the Rudolph L. Baer Professor in the Ronald O. Perelman Department of Dermatology, professor in the Departments of Medicine and Urology, and associate dean for translational research support. This project focuses on developing a predictive tool that enables clinicians to minimize exposure of patients with resected stage III/IV melanoma to severe toxicity while maximizing clinical benefit from immune checkpoint inhibitors. The researchers plan to identify autoimmune susceptibility to developing immune-related adverse events. They also hope to establish whether prophylactic infliximab mitigates development of gastrointestinal toxicity from immunotherapy in patients identified as being at high risk of developing those adverse events.

Project 4 explores the role of microRNAs in relapse following immunotherapy in patients with stage II melanoma. It is co-led by David Polsky, MD, PhD, the Alfred W. Kopf, MD, Professor of Dermatologic Oncology and director of the Pigmented Lesion Service in the Ronald O. Perelman Department of Dermatology and professor of pathology; and Eva M. Hernando-Monge, PhD, associate professor and vice chair for science in the Department of Pathology. This project aims to use microRNAs to optimize the clinical management of patients with stage II melanoma.

A preliminary study by Dr. Hernando-Monge measured expression levels of microRNAs in patients who had long-term survival or died after resection of their tumors. She and her colleagues generated microRNA "signatures" that accurately identify which patients are at high risk of relapse and death. To refine the microRNA signature, the SPORE project is analyzing a new cohort of patients enrolled at NYU Langone who are more representative of the intended use population.

"Patients with stage II melanoma have a 25 percent risk of death over the long term, and it is important for us to try and move adjuvant therapy to these patients," Dr. Polsky says. "We think that our work can help identify which patients really need immunotherapy and spare patients the risk of the toxicity if they don't need it."

A TEAM EFFORT

The SPORE grant is the culmination of nearly two decades of work developing a melanoma biospecimen repository by the Interdisciplinary Melanoma Cooperative Group (IMCG), a multidisciplinary, translational melanoma research program. Established by Dr. Osman in 2002, IMCG includes 24 investigators representing 10 departments at NYU Langone and has enrolled close to 5,000 patients. The blood, tissue specimens, and clinical information the program has collected provide an unparalleled resource to study how to improve melanoma treatment. Expertise in pathology and biostatistics is crucial.

"NYU Langone has been recognized as a referral center for skin cancer since the 19th century," Dr. Osman says. "There is a legacy we are building on."

"The SPORE grant is a team effort of many investigators over the years and is built on a broad patient base and the matching expertise of clinicians at NYU Langone," Dr. Weber adds.

Disclosures: Jeffrey S. Weber, MD, PhD, consulted for Bristol-Myers Squibb and Merck, and accepted travel reimbursement from both. He was named on a PD-1 biomarker for outcome by Biodesix and named on an ipilimumab biomarker for outcome by Moffitt Cancer Center.

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Within High-Risk Cancer Genetics Program, Prevention Starts with Maximizing Screening's Potential

The High-Risk Cancer Genetics Program (HRCGP) at Perlmutter Cancer Center is reshaping strategies for genetic risk assessment for cancer to better identify those who could benefit from testing. With enhanced methods to capture high-risk patients, experts hope to be able to intervene earlier to prevent the disease or detect it at an earlier, more curable stage.

REIMAGINING GENETIC SCREENING METHODS

Innovations from the program, such as a novel delivery model for genetic screening, have fostered enhanced collaboration to increase patient access to genetics services.

The delivery model was developed with collaborators at the Huntsman Cancer Institute and adapted for NYU Langone Health by Devin Mann, MD, MS, associate professor of population health and medicine, and teams at the Healthcare Innovation Bridging Research, Informatics, and Design (HiBRID) and Digital DesignLab (DDL).

As the landscape of genomics and clinical genetics evolves rapidly, thanks to advancements in basic and translational research, the program team has implemented continuous quality improvement initiatives to keep pace with frequently changing guidelines developed by the National Comprehensive Cancer Network (NCCN). Recently, this new virtual health model proved its mettle as new prostate cancer testing guidelines were implemented by the NCCN. The updated guidelines stipulate that any man with advanced prostate cancer automatically qualifies for genetic testing.

"We knew in advance that the NCCN planned to revisit the guidelines," notes program director Ophira M. Ginsburg, MD, associate professor of medicine and population health. "With our advanced use of technology and innovative service models, we were able to rapidly mobilize to offer testing for this population."

BROADENING RISK IDENTIFICATION'S REACH

The center's focus on rapid development of innovative strategies to bring relevant screening to more patients is a response to underutilization of screening services by patients who meet the criteria, notes Dr. Ginsburg. "At least 50 percent of people who would qualify for genetic testing under the guidelines aren't identified as potentially high-risk or are otherwise not offered genetic testing—despite declining costs and increasing insurance coverage for such services," she says.

To increase the utilization of genetic screening services, the HRCGP team actively stays up-to-date with rapidly evolving research and guidelines, leads educational initiatives for NYU Langone faculty and students, and trains the next generation of clinical providers, including genetic counseling students. Cancer genetic counselors actively participate in tumor boards, providing genetics expertise that is an increasingly vital part of cancer care.

For example, when a multigene panel identifies a potential gene variant that may signal a risk of developing pancreatic cancer, genetic counselors will refer patients to the Pancreatic Cancer Early Detection and Prevention Center at Perlmutter Cancer Center's Pancreatic Cancer Center, directed by Diane M. Simeone, MD, the Laura and Isaac Perlmutter Professor of Surgery (see sidebar). The relationship, Dr. Ginsburg says, is bilateral.

"If Dr. Simeone's team identifies a high-risk family with a BRCA2 mutation, they will deal with the pancreatic cancer–related clinical management," she says. "Then they refer that individual or the family members who need counseling for other implications of BRCA2. It's a seamless operation."

CANCER "MOONSHOT" GRANT TAKES AIM AT SCREENING BARRIERS

Identifying individuals who have inherited cancer susceptibility can be critical for tailoring cancer prevention, screening and treatment strategies, adds Dr. Ginsburg. "Genetic testing efforts focused mainly on people with cancer can leave out individuals at high risk who don't have a close relative currently undergoing cancer treatment," she says. "This is a really big gap. We're missing most of the people out there who really can benefit from cancer genetic services."

Ophira M. Ginsburg, MD and John G. Pappas, MD

PHOTO: NYU LANGONE STAFF

Early Detection and Prevention Initiative Seeks to Increase Pancreatic Cancer Survival Rate over Next 10 Years

The five-year survival rate for patients with pancreatic cancer is about 9 percent, at least in part because the disease has typically spread to other organs by the time it is diagnosed. The Pancreatic Cancer Early Detection and Prevention Center, part of NYU Langone's Perlmutter Cancer Center, brings together clinicians, researchers, and patients, with the goal of increasing the five-year survival rate of pancreatic cancer to 50 percent within the next 10 years.

There are currently 15 genes known to be associated with the risk of developing pancreatic cancer, and additional genetic risk factors remain to be discovered. About 13 percent of pancreatic cancer patients have a germline mutation that increases pancreatic cancer risk, even in the absence of a positive family history. Diane M. Simeone, MD, director of the Pancreatic Cancer Center, partnered with the American Society of Clinical Oncology to implement a new guideline that calls for all patients with pancreatic cancer to receive germline testing.

"We are now learning that certain germline mutations are associated with much better therapeutic responses to certain types of drugs than others, so this information can be of direct benefit to our pancreatic cancer patients," says Dr. Simeone, who is the Laura and Isaac Perlmutter Professor of Surgery and professor of pathology. "We want to increase identification of family members who are at increased risk, so that they can be enrolled in early detection programs." The Pancreatic Cancer Early Detection and Prevention Center currently follows more than 250 patients at high risk for pancreatic cancer with annual imaging. Studies have found that screening in high-risk individuals increases the chance of detecting a resectable lesion from 15 percent to 90 percent.

Under the direction of Dr. Simeone and her team, NYU Langone serves as the coordinating center for the newly formed PRECEDE (Pancreatic Cancer Early Detection) Consortium, a collaborative of 35 academic centers around the country and world focused on early detection in familial high-risk individuals. With founding support from Project Purple, the consortium has established a shared data platform that will open for use early this year. The PRECEDE Consortium expects to enroll more than 3,000 high-risk individuals with standardized collection of data and biosamples to drive critical early detection research in a variety of areas, including biomarker validation, comprehensive risk modeling, and risk communication.

To help patients determine their risk of developing pancreatic cancer, Perlmutter Cancer Center's Pancreatic Cancer Center, in partnership with the University of Michigan Rogel Cancer Center, has developed a pancreatic cancer risk assessment tool. If the tool suggests that someone has certain risk factors, they can be put in touch with a genetic counselor and pancreatic cancer specialists at Perlmutter Cancer Center.

Diane M. Simeone, MD

PHOTO: NYU LANGONE STAFF

"In order to meet the goal of increasing the five-year survival rate, we really need to move the needle in the early detection of pancreatic cancer," Dr. Simeone says.

Dr. Ginsburg is co-principal investigator of a 2018-launched "cancer moonshot" study funded by the NCI through a five-year, $5 million grant. Working with the Huntsman Cancer Institute at the University of Utah, the High-Risk Cancer Genetics Program will use a clinical decision support tool embedded within electronic medical records to automatically identify cancer-free patients in the primary care setting who qualify for genetic testing.

The BRIDGE (Broadening the Reach, Impact, and Delivery of Genetic Services) study will randomize patients from 48 clinics in Salt Lake City and New York City.

The study has the capacity to identify factors that influence whether people who are identified through clinical decision support algorithms follow through with testing services. The researchers also plan to compare rural and urban communities in Salt Lake City with the NYU Langone catchment area, which includes a much more diverse population. The team is also preparing to pilot this service for individuals from ethnocultural minority groups, including Latin and Spanish-speaking patients.

"We're only seeing the tip of the iceberg of the high-risk population in and beyond New York—even where multiple centers offer reasonable access to genetics services," says Dr. Ginsburg. "The primary objective of this project targets suboptimal referrals from busy primary care practices, by offloading that task from primary care providers to a semi-automated program."

MAKING SENSE OF GENETIC MARKERS

At the other end of the diagnostic spectrum, the increasing proliferation of direct-to-consumer genetics testing can mislead patients with incomplete disease risk information that lacks the in-depth genetic analysis needed to fully understand cancer risk. "Buyer beware: You could end up with a false sense of reassurance," Dr. Ginsburg warns.

In prostate cancer, for example, the most common genetic mutation that confers risk is BRCA2, but a panel that screens for up to 12 target genes is available for men with locally advanced or metastatic prostate cancer, regardless of ethnicity, family history, or age of diagnosis.

"There are often discordant results even between CLIA-certified, New York State-approved labs," Dr. Ginsburg says. "It's not their fault, it's just complicated, as there is a lot of new information coming at us because of the advent of multigene panels." For example, with increasing numbers of results that include more than one "VUS", or variant of uncertain significance, often such VUS are re-classified, usually from VUS to benign—but occasionally a variant is upgraded to pathogenic. "Fortunately, the labs we use notify ordering physicians of all reclassifications," adds Dr. Ginsburg. "Our team follows up with our patients to ensure that they and their providers have the most up-to-date revised results and understand their meaning."

To ensure that patients subsequently receive the best care based on test results, the program team reviews the most complex cases during a weekly clinical cancer genetics case conference. The expertise of clinical geneticist John G. Pappas, MD, an associate professor of pediatrics, has proven crucial in interpreting more complex test results, and in navigating family histories that suggest a syndrome that might include non-cancer issues, Dr. Ginsburg adds.

For more on this story and other topics, visit **nyulangone.org/cancer2019**

Neuro-oncologist Dr. Sylvia C. Kurz is part of a team of researchers at Perlmutter Cancer Center running Phase 2 clinical trials that provide new options for treating glioblastomas and meningiomas.

PHOTO: NYU LANGONE STAFF

Clinical Trials Target Difficult to Treat Brain Tumors

A pair of multicenter clinical trials at NYU Langone targeting two vastly different types of brain tumors—glioblastoma and meningioma—are offering patients with both conditions opportunities for access to novel treatments.

TARGETING A DOPAMINE RECEPTOR TO ELIMINATE GLIOBLASTOMA TUMORS

Glioblastomas, the most common malignant intracranial brain tumors, are highly aggressive cancers with limited treatment options. At NYU Langone's Perlmutter Cancer Center, a Phase 2 trial is evaluating the investigational drug ONC201, which targets the small subset of glioblastoma patients who have failed chemotherapy and whose tumors have a histone H3 K27M mutation. These mutations, which comprise only a few percent of glioblastomas, occur in young adults, typically people in their 20s through 40s, and appear in midline structures within the central nervous system.

Since the trial opened in 2017, NYU Langone has enrolled 17 patients—the most of any of the centers conducting the trial. Two patients have had partial responses and one patient had a near-complete response, which has been sustained for nearly two years since beginning this drug.

"For glioblastoma patients, there are very few promising actionable targets that are currently being explored in clinical trials," says Sylvia C. Kurz, MD, PhD, principal investigator and assistant professor of medicine and neurology. "In general, the natural history of these tumors is that once they have failed radiation and traditional chemotherapy, there's usually nothing that stops their growth."

AN ANTIBODY FUSED TO A RADIONUCLIDE TARGETS MENINGIOMA TUMORS

Meningiomas are the most common benign intracranial tumors; nevertheless, about 10–15 percent of cases demonstrate aggressive clinical behavior. In July 2019, a Phase 2 clinical trial opened at Perlmutter Cancer Center for patients with intracranial and spinal meningiomas that are unresectable and/or have progressed despite prior therapies. The trial uses a radionuclide-linked antibody, 177Lutetium-dotatate, or Lutathera, that targets somatostatin receptor type 2, which is expressed in approximately 95 percent of all meningiomas.

Perlmutter Cancer Center is the first United States site for what will be a multicenter study led by its investigators. Later this year and next, University of Pittsburgh Medical Center, Cleveland Clinic, and Weill Cornell Medical Center are expected to begin enrolling participants. Dr. Kurz is co-chair investigator with Elcin Zan, MD, assistant professor of radiology. Erik P. Sulman, MD, PhD, professor of radiation oncology, co-director of the Brain and Spine Tumor Center, and vice chair for research in the Department of Radiation Oncology, is overall principal investigator.

The Lutathera trial has generated interest from patients around the country, as well from investigators interested in opening subsites of the trial at their institutions.

"For patients with progressive meningiomas, there are no established medical treatment options available that have been demonstrated to be effective," says Dr. Kurz. "Because there is only a limited number of clinical trials available, this is a great opportunity to offer a clinical trial to this patient population."

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Between them, thoracic surgeons Dr. Robert J. Cerfolio and Dr. Michael Zervos have completed more than 3,000 robotic surgeries, advancing this treatment for lung cancer.

PHOTO: NYU LANGONE STAFF

Leading the Way in Robotic Surgery for Lung Cancer

Over the past decade, multiple studies have shown that robot-assisted surgery for lung cancer decreases postoperative morbidity, pain, and recovery time compared to thoracotomy; several reports indicate potential advantages over other minimally invasive techniques as well, including improved lymph node harvesting and lower blood loss. NYU Langone Health is at the forefront of research and clinical innovation aimed at advancing this modality.

PIONEERING ROBOTIC APPROACHES TO SEGMENTECTOMY AND SLEEVE RESECTION

A growing body of evidence suggests that for early-stage lung cancer with small tumors, segmentectomy can lead to greater patient quality of life than more extensive surgery, while producing comparable oncologic outcomes. In March 2019, researchers led by Robert J. Cerfolio, MD, MBA, director of clinical thoracic surgery and of Perlmutter Cancer Center's Lung Cancer Center, and senior vice president, vice dean and chief operating officer, published a study in *Annals of Thoracic Surgery* reviewing a consecutive series of 245 of his patients who underwent thisprocedure robotically—the largest series of minimally invasive segmentectomies to date.

They reported a 100 percent R0 resection rate, and a median number of 17 lymph nodes resected by five N2 and three N1 stations. Median operative time was 86 minutes, and average length of stay was 2.1 days. Although seven of the first 100 patients required conversion to robotic lobectomy, none were for bleeding and there were no conversions to lobectomy or thoracotomy thereafter. There was no 30- or 90-day mortality. "This study shows that robotic segmentectomy offers outstanding safety and perioperative outcomes," Dr. Cerfolio observes.

Dr. Cerfolio has also pioneered robotic techniques for sleeve resection of the airway, one of the most challenging procedures in lung cancer surgery. In November 2019, he and colleagues presented a paper outlining these evolving methods at the Southern Thoracic Surgical Association (STSA) annual meeting in Marco Island, Florida. The paper retrospectively reviewed Dr. Cerfolio's robot-assisted sleeve resections from April 2013 to April 2019, following 23 consecutive patients—one of the largest known case series in the world for this procedure.

These patients underwent resection of the airway with or without pulmonary resection and/or pulmonary artery resection. Median operative time was 211 minutes, median number of resected lymph nodes was 23, and median length of stay was three days. There were no 30- or 90-day mortalities. At 18 months follow-up, no patients had an anastomotic stricture and there were no recurrent cancers.

Approximately 98 percent of lung resections are performed minimally invasively as opposed to open techniques at NYU Langone, one of the highest rates in the world. The effectiveness of the thoracic team's approach is reflected in a variety of metrics. Surgeons at the Lung Cancer Center achieve exceptional rates of lymph node removal, averaging 25 from the right chest and 19 from the left (including five N2 and at least two N1 stations on each side). For lobectomies, the median blood loss is 20 mL, among the lowest on record. The median postoperative length of stay is two days, less than half the national average. The team reports a 30-day mortality rate of less than 0.2 percent for lobectomies—also a fraction of the norm.

Over the past 20 years, Dr. Cerfolio has performed nearly 18,000 lung surgeries, making him one of the most prolific practitioners in his field. He and Michael Zervos, MD, clinical associate professor of cardiothoracic surgery, chief of thoracic surgery and director of robotic thoracic surgery at Tisch Hospital/Kimmel Pavilion, have completed over 3,000 robotic surgeries between them, and teach their innovative techniques to clinicians around the globe. "Patients come to us from every corner of the planet," Dr. Cerfolio notes, "and hundreds of surgeons have come to observe the incredible technical expertise of our entire team."

Recognition for Highest Quality of Care in Lobectomies

In 2019, NYU Langone Health earned a three-star rating from the Society of Thoracic Surgeons (STS) for its care of lung cancer patients who undergo lobectomy. This ranking denotes the highest category of quality among practices in the United States and Canada. Only seven of 199 hospitals received a three-star rating, which was based on an analysis of outcome data compared to the overall average for lobectomies performed by participants in the STS General Thoracic Surgery Database from January 2016 to December 2018.

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Phase 1 Clinical Trials Provide Access to Novel Treatments

Established five years ago, the Phase 1 Drug Development Program at NYU Langone Health's Perlmutter Cancer Center has grown to offer nearly 40 Phase 1 clinical trials, with 10 new trials since March 2019, that cover a wide array of drug strategies and tumor types.

"A cancer center that provides access to the most novel, cutting edge therapies for its patients can enrich all the other disease groups," says Daniel C. Cho, MD, associate professor of medicine and director of Perlmutter Cancer Center's Phase 1 Drug Development Program. "For example, a successful Phase 1 trial might lead to subsequent trials in lung cancer, melanoma, bladder cancer, and other diseases."

A NOVEL IMMUNOTHERAPY DRUG WITH THE PROMISE OF TREATING A BROAD RANGE OF CANCERS

Immunotherapies comprise the bulk of Phase 1 trials offered at Perlmutter Cancer Center, including a first-in-human clinical trial in solid tumors targeting the Siglec-15 pathway, an important immune suppressor in the PD-L1 null tumor microenvironment. This exciting trial is currently underway at Perlmutter Cancer Center and four other sites in the United States.

Agents targeting the PD1/PD-L1 immune checkpoint axis (or pathway) have revolutionized the treatment of melanoma and some other solid tumors. Unfortunately, however, with the exception of a fraction of melanomas, other solid tumors respond only transiently or not at all. Preclinical research by Jun Wang, MD, assistant professor of pathology, indicates that tumors with high levels of PD-L1 tend to have low Siglec-15 expression, whereas tumors low in PD-L1 tend to have high Siglec-15. Overall, only about 3 percent of tumors express both markers. Since patients with tumors high in PD-L1 tend to be the group that responds to PD-1/PD1 inhibitors, a therapy that selectively targets the PD-L1 low population could significantly increase the number of patients who benefit from immunotherapy.

TARGETING A SPECIFIC MUTATION IN KRAS

Perlmutter Cancer Center will be a site for several studies on a KRAS inhibitor that targets the so-called "G12C" mutation in KRAS, one of the most frequently mutated oncogenes in all cancer. This mutation accounts for 12 percent of all KRAS G12 mutations and 40 percent of KRAS mutations in non-small-cell lung carcinomas.

"We have struggled to target KRAS since the advent of oncology, so having a drug that can be effective in the particular subset of this mutation is very exciting," Dr. Cho says.

NKTR-214 TRIAL LEADS TO LATER PHASE TRIALS

One of the program's more exciting studies, Dr. Cho says, is a Phase 1 trial of an immunotherapy drug called NKTR-214, a novel "pegylated" version of IL-2, which is being studied in combination with nivolumab or ipilimumab and nivolumab across several different tumor types. This novel approach, which combines an immune checkpoint inhibitor with a cytokine driver to deepen the response, has led to two Phase 3 trials in melanoma and renal cancer and two Phase 2 trials in lung and bladder cancer.

Nearly all of the Phase 1 trials are sponsored by pharmaceutical companies. However, Perlmutter Cancer Center is one of the lead sites on a UM1 application for an early therapeutics grant that would provide membership in the NCI's Experimental Therapeutics Clinical Trials Network. ET-CTN membership, in turn, would provide grant support to conduct investigator-initiated trials under the auspices of the Cancer Therapy Evaluation Program.

"Drug development has evolved to the point where most trials are either Phase 1 or Phase 3, with fewer Phase 2 trials than there used to be," Dr. Cho says. "This grant presents an opportunity for cancer centers who devote resources to Phase 1 studies to get involved early on and make a substantial and substantive impact on not just drug development, but patient care."

For more on this story and other topics, visit
nyulangone.org/cancer2019

Daniel C. Cho, MD

PHOTO: NYU LANGONE STAFF

One Patient's Story with the NKTR-214 Trial

Karen Peterson, a patient with triple-negative breast cancer (TNBC), did exceedingly well with NKTR-214. Diagnosed with Stage I disease in 2015, Ms. Peterson's cancer became metastatic two years later. She identified an immunotherapy trial for breast cancer at Perlmutter Cancer Center, and received a call from Dr. Cho, who suggested she wait for the NKTR-214 trial to open. After 20.7 months of treatment, Ms. Peterson reached maximum clinical benefit with a 100 percent reduction in her target tumors—and continues to show disease stability. This outcome has resulted in a planned Phase 2 trial for NKTR-214 in TNBC.

PHOTO: SASHA NIALLA

Selected Publications

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Awards & Recognition

Shruti Naik, PhD, received a two-year V Foundation V Scholar grant for her project, "Uncovering the Role of Inflammatory Memory in Tumorigenesis."

Jeffrey S. Weber, MD, PhD, received the Melanoma Research Foundation's Humanitarian Award.

Eva Chalas, MD, was appointed to lead the American College of Obstetricians and Gynecologists, the premier national organization dedicated to women's health.

Xue-Ru Wu, MD, led the team that received a five-year P01 grant from the National Cancer Institute (NCI) to study molecular tumorigenesis of bladder cancer.

Paul E. Oberstein, MD, received a NCI 2019 Cancer Clinical Investigator Team Leadership Award.

Jane Skok, PhD, received an NCI P01 grant to study the impact of changes in chromatin architecture on cancer phenotypes and tumor progression.

Liam J. Holt, PhD, was one of seven winners of the 2019 Pershing Square Sohn Prize for Young Investigators in Cancer Research.

Vamsi Velcheti, MD, was named a member of the American Society of Clinical Oncology's 2020 Leadership Development Program.

Dafna Bar-Sagi, PhD, was elected a Fellow of the American Association for Cancer Research Academy.

Sylvia Adams, MD, was elected co-chair of the Breast Immuno-Oncology Task Force of the NCI Breast Cancer Steering Committee.

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NYU Langone has achieved top rankings by Vizient, and is the only full-service health system in New York City with an "A" Leapfrog safety grade and a CMS 5-star rating in 2020. These accolades are reflective of a shared culture of quality that permeates our growing network, now inclusive of NYU Winthrop Hospital and its ambulatory sites on Long Island. All of our sites are held to the highest quality standards set at an institutional level.

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We are focused on research that will improve standards of practice—and ultimately patient outcomes. We've recently made advances in bladder cancer treatment, melanoma research backed by a large NCI SPORE grant, and an innovative genetic screening program.

2019 HIGHLIGHTS
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