Transformative Treatments
for Head and Neck Cancers

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New life-saving advances in treatment for head and neck cancers, as well as the FDA’s approval of pembrolizumab, stem from research done by physician-scientists at Yale, particularly through the leadership of Barbara A. Burtness, MD. Dr. Burtness directed a large, international, randomized phase III clinical trial whose results persuaded the FDA to approve the new treatment.

A Patient Partnership in Care and Research

For the past 16 years, Dick Metz has experienced the ups and downs of a cancer diagnosis. He has had clean scans and bad scans, and has experienced joys and disappointments of therapy results, but he has never faltered. Mr. Metz’s journey illustrates the incredible strides that have been made in treating melanomas.

New Paradigm for Immunotherapy

Two scientists at Yale Cancer Center are developing a new paradigm for immunotherapy. It could radically improve and expand current approaches by moving beyond checkpoint inhibitors that target specific biomarkers in a few types of cancer. Their research moves upstream of T-cells, beyond the adaptive immune system, to the innate command center—the innate immune system.

Following the Biology to Develop New Clinical Trials for Young Adults

A new clinical trial launched from Yale exemplifies innovation at every stage on the long journey, beginning with a breakthrough in the lab to an application in the clinic, with stops to pick up collaborators, funders, and institutional partners. The trial is also significant for its focus on a group usually overlooked by cancer research—adolescent and young adult patients.

Ten years ago, Smilow Cancer Hospital opened its doors to our patients bringing together all inpatient and outpatient care and our entire clinical cancer care enterprise into one building. The opening of Smilow transformed the way we delivered cancer care to our patients and at the same time, catapulted our clinical research operations, enabling the next generation of discoveries in cancer therapeutics. In the last decade, immunotherapy has outpaced chemotherapy in breakthroughs and new FDA approvals, and our physicians and scientists at Smilow Cancer Hospital and Yale Cancer Center have led the development for many of these groundbreaking innovations.

The transformative research in head and neck cancers and recent new drug approvals have substantially improved outcomes for patients with these malignancies. Dr. Barbara Burtness has led the international clinical trials providing the data to make these treatments available and she continues to lead the field with new clinical trials combining therapies and providing new options for our patients.

Dr. Ranjit Bindra is building off of unprecedented discoveries from his laboratory to launch a new clinical trial for young adult patients with gliomas at Smilow Cancer Hospital. He discovered that tumors with IDH1/2 mutations, including 30-40 percent of adolescent gliomas, were responsive to olaparib. He then partnered with Dr. Asher Marks, a pediatric oncologist, to assemble this unique clinical trial to test the research—which is now providing a novel treatment approach for patients.

Dr. Carla Rothlin and Sourav Ghosh are developing a new paradigm for immunotherapy and the excitement is mounting around their research. Beyond the current use of the adaptive immune system in PD-1/L1 therapies, Drs. Rothlin and Ghosh are leveraging the innate immune system and arming T-cells to bolster the immune response to cancer. We look forward to sharing their progress as their research moves from their lab and into our clinics.

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Research efforts like Dr. Rothlin and Dr. Ghosh’s and laboratory to clinic partnerships like Dr. Bindra and Dr. Marks’ are illustrations of the power of collaborative team science at Yale Cancer Center and Smilow Cancer Hospital—initiatives that impact patient care and advance cancer treatment every day. Together, our scientists and clinicians work to ensure we are continually innovating to benefit cancer patients worldwide. Smilow Cancer Hospital’s 10th anniversary provides us with an opportunity to reflect on the tremendous accomplishments of the past decade, and to plan for exciting progress in the coming years. I look forward to sharing more from our anniversary year in the coming months, and to celebrating our successes with you.

Sincerely,

Charles S. Fuchs, MD, MPH
Director, Yale Cancer Center and Physician-in-Chief, Smilow Cancer Hospital
In June, for the first time in a decade, the FDA approved a new first-line treatment for patients with metastatic or recurrent head and neck cancer (HNC). These cancers are notoriously difficult and painful to treat, typically with poor outcomes, so a new approach was overdue. This treatment uses the immunotherapy drug pembrolizumab (Keytruda) for patients with metastatic or recurrent HNC, either alone or in combination with chemotherapy. The new regimen improves on the old standard of care (three chemotherapy drugs) by dramatically improving survival rates, both short-term and long-term. When it is given alone, it is also significantly less toxic.

These life-changing advances, as well as the FDA’s approval, stem from research done by physician-scientists at Yale, particularly through the leadership of Barbara A. Burtness, MD, Professor of Medicine and Co-Leader of the Developmental Therapeutics Research Program. Dr. Burtness directed a large, international, randomized phase III clinical trial whose results persuaded the FDA to approve the new treatment.

Pembrolizumab is an immune checkpoint inhibitor that blocks the expression of PD-L1, a protein that camouflages cancer cells and allows them to elude the immune system. By blocking PD-L1, pembrolizumab strips away cancer’s camouflage. The immune system then detects the invaders and attacks. Not all tumors express this biomarker, and some express it at low levels.

The trial, directed by Dr. Burtness, involved almost 900 patients divided into three groups: one received pembrolizumab alone, another was treated with pembrolizumab plus chemotherapy, and a third was given the older standard treatment of chemotherapy plus an antibody called cetuximab. The patients had varying levels of PD-L1.

Dr. Burtness presented the interim findings in Munich last October at the annual meeting of the European Society for Medical Oncology (ESMO). The data were clear: Patients who received pembrolizumab did better than those who did not.

Since then, Dr. Burtness and her colleagues have been digging deeper into the data. In June, updated findings were presented at the annual meeting of the American Society of Clinical Oncology (ASCO). The researchers looked specifically at the two groups of patients who received chemotherapy—one with pembrolizumab and the other with the standard of care. They broke down the results according to the patients’ expression of PD-L1. Among those with higher levels of PD-L1, the addition of pembrolizumab to chemotherapy made a large difference in median survival—14.7 months compared to 11 months for patients on the standard regimen.

“That was very statistically significant,” said Dr. Burtness. “The other remarkable thing was the durability of the effect.” After two years, 35 percent of the people who had received...
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“Then we looked to see if there were subgroups that didn’t seem to benefit from pembrolizumab,” said Dr. Burtness. “But every single subgroup we looked at—whether based on age, gender, or performance status or region of the world...or whether they had HPV [human papillomavirus], or whether they had recurrent disease only or also had metastatic disease—across all those groups, pembrolizumab had survival rates were 33 percent and eight percent, respectively.

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Meanwhile, Dr. Burtness is immersed in additional clinical trials concerning HNC. One involves patients who are radiotherapy-resistant. The standard of care for these patients is major surgery, often with terrible after effects, and their cancer typically recurs quickly. In the trial at Yale, patients receive four doses of pembrolizumab before surgery. “The hope is that the immunotherapy will reverse the exhaustion of the patient’s immune system and allow it to recognize the cancer again so that the operation can be more successful,” explained Dr. Burtness. She added that it’s too early to discuss results, but notes that some responses have been remarkable.

Another trial beginning this fall will treat HNC with a combination of immunotherapy and an HPV vaccine. Her lab is also exploring targeted therapies, which haven’t been individually successful against HNC. But in a paper published in February in Clinical Cancer Research, she and colleagues found that simultaneously targeting and inhibiting two oncogenic kinases, Aurora Kinase A (AURKA) and WEE1, creates a spectacular synergistic response in the HNC squamous cell carcinoma. “The cells kind of explode,” said Dr. Burtness. “It looks like a nova.” The researchers have demonstrated this destructive synergy in HNC cell lines and mouse models, and hope to move into a clinical trial shortly. “It’s pretty exciting,” said Dr. Burtness.
Mr. Metz's chronic leukemia began in 2003 when his dermatologist biopsied a mole on his back and discovered stage II melanoma. Mr. Metz was referred to surgeon, Stephan Artyain, MD, MBA, where he underwent wide excision surgery, which removes the tumor and a margin of assumed healthy tissue around it. In addition, nearby lymph nodes were checked and a biopsy was taken of the sentinel lymph node, the lymph node that drains the tumor. For Mr. Metz, all lymph nodes were found to be clear and he finally felt that he could exhale. He was then referred to Harriet Kluger, MD, Professor of Medicine (Medical Oncology), to be monitored periodically for the next three years for scans and checkups. "All levels, I might be able to enter the TIL study."

The doctors had me check in with them each year to make sure nothing had spread to other organs in my body. All was fine until a few years later when I started waking up in the middle of the night due to night sweats."

Mr. Metz's primary doctor sent him for an ultrasound, which revealed an 11-centimeter tumor on his liver, later determined to be a metastasis from the melanoma on his back. "I was shocked and surprised that the melanoma cells had escaped into the bloodstream and gone from my back to my liver years later," Mr. Metz said.

"Dr. Kluger explained that if we did not do anything, I only had a matter of months to live. This news sent me into a tailspin. I came out of it in what I call my fight mode. I wanted to become an expert in my disease. I immediately went on the internet to find out any information I could. I wanted to really understand my options and what possible treatments could beat this disease."

The choices of treatment for stage IV melanoma in 2008 were very limited, either chemotherapy—which had limited success, or a form of immunotherapy—high-dose interleukin-2, which required two five-day hospital stays, with one week off in between, followed by scans to see the results of the treatment. Mr. Metz chose to proceed with the interleukin-2, but after completing the treatment, his scans did not show any changes in the tumor.

Dr. Kluger recommended that Mr. Metz visit the National Cancer Institute (NCI) in Bethesda, Maryland for an investigational treatment where he would be considered for a clinical trial for tumor infiltrating lymphocyte therapy (TIL), which activates immune cells to recognize and attack cancer cells. This modality was not available at the time at Yale, but it is now.

Unfortunately, Mr. Metz’s blood test revealed high liver enzyme levels from the tumor in his liver, which indicated he was not a candidate for the TIL investigational trial. Instead, the doctors at the NCI recommended surgery to remove as much of the tumor on his liver as possible. They also explained that there was a small chance (15-20 percent) he would not survive the surgery. Considering his chances of survival without surgery were 2-3 months, it was an easy decision. "The liver is one organ that can actually grow back," explained Mr. Metz. "The doctors told me that taking out the tumor would allow the liver to recover, and with normal liver enzyme levels, I might be able to enter the TIL study."

Following the surgery, Mr. Metz continued to return to Bethesda periodically for the next three years for scans and checkups. "All was well," said Mr. Metz, "until a scan showed that the melanoma had metastasized to my brain. I was devastated because I had been thinking that if something happened, the TIL treatment would be my savior. And now brain mets (metastases) would preclude me from getting that treatment."

Mr. Metz called Dr. Kluger, who explained the available options and introduced him to Veronica Chiang, MD, FAANS, Professor of Neurosurgery, in March 2011. After further consultation, Dr. Chiang recommended he be scheduled for a Gamma Knife procedure. The Gamma Knife treatment allows a team of radiation therapists and neurosurgeons to give high doses of radiation to a very targeted area of the brain. "After the treatment, my life pretty much went back to normal again."

It was at this time that Mr. Metz wanted to make a difference. He launched The Brain Metastasis Fund to further support Yale Cancer Center’s research efforts. "My doctors had been great to me and I wanted to give back. I relied on my former experience working in the insurance and financial industries to begin the initiative. I invited 100 people to a party in my backyard. Seventy-five showed up and we started raising money. To date, we have raised over $700,000 from private donations," said Mr. Metz.

In fact, one of the major research initiatives resulting from The Brain Metastasis Fund was to support Yale Cancer Center initiated clinical trials that provide access to promising drugs prior to their approval by the FDA. One such class of immunotherapy was looking highly promising at the time, but patients with brain metastases were traditionally excluded from those trials. Therefore, the team at Yale used the funding to initiate the first study of pembrolizumab for patients with brain metastases from melanoma or lung cancer. In 2014, Mr. Metz was accepted into the clinical trial.

After starting on pembrolizumab, which at the time was a much higher dose of the drug than what is used today, no brain metastases developed. However, Mr. Metz could not tolerate the higher dosage and he was taken off the trial and instead placed on the FDA-approved dosage of pembrolizumab, which allowed stabilization of the disease and for Mr. Metz to recover functionally to where he is today.

"I have the highest regard for Dr. Kluger. She is incredibly smart and talented. And she's never given up on me. She continues to find new ways to keep me going. Today, I'm still on pembrolizumab along with phenobarbital to lessen the side effects. If it wasn’t for her and her team, I would not be alive today.”

Mr. Metz cherishes the encouragement and assistance that his wife of 46 years, his two sons, and his grandchildren have given him. "They continue to be my greatest joy. I treasure the time I spend with my family. My cancer has changed my perspective and my life. I have looked at myself and set new priorities. I am fortunate to be surrounded by good doctors, a wonderful family, and many friends. I know that there is a tremendous amount of work being done in the research field. That gives me hope that someday I will be totally healed."
When the immune system detects a disruption of the status quo—an injury, an infection—it sends T-cells and B-cells to overpower the invader. But cancer cells can avoid these protectors by sending out chemical signals that lull, confuse, or even stop the immune response.

Researchers have recently succeeded in countering this trickery with drugs called checkpoint inhibitors. The inhibitors block the cancer cells’ misleading signals, enabling the immune system to wake up and fight the invaders. These new immunotherapies can be miraculously effective against certain cancers with specific biomarkers, most notably PD-1/PD-L1.

That’s very good news for some cancer patients. Unfortunately, many cancers—including brain, breast, ovarian, pancreatic, and colon—do not respond to current checkpoint inhibitors. Among all cancer patients, only about 14 percent are helped by the new immunotherapies. In some cases, a strong initial response fades away as the cancer develops resistance to the inhibitor.

Two scientists at Yale Cancer Center are developing a new paradigm for immunotherapy. It could radically improve and expand current approaches by moving beyond checkpoint inhibitors that target specific biomarkers in a few types of cancer.

“This approach is not the next anti-PD-L1,” said Carla Rothlin, PhD, Dorys McConnell Duberg Professor of Immunobiology and Pharmacology and Howard Hughes Medical Institute Faculty Scholar. “It’s a completely different way of thinking about how to increase anti-tumor responses from the immunological side.”

“The concept evolved out of our studies of the fundamental principles that regulate the immune response against viruses, bacteria, and so on,” added Sourav Ghosh, PhD, Associate Professor of Neurology and of Pharmacology. “Now we are applying this fundamental understanding to cancer. Unlike checkpoint inhibitors, these new approaches should be applicable to many types of cancer, not just lung cancer or colon cancer.”

Current immunotherapies work by re-activating T-cells that have been put to sleep. T-cells are specialists, trained to recognize and attack specific antigens. Their narrow focus is their strength. But cancer cells exploit this specialization by emitting a signal that prevents a T-cell from reacting against its particular target. When a checkpoint inhibitor blocks the false signal, T-cells wake up and attack. T-cells, like B-cells, are part of the adaptive immune system.

Drs. Rothlin and Ghosh want to move upstream of T-cells, beyond the adaptive immune system, to the innate immune system. It’s older and more primitive, and it’s primary. It activates the adaptive immune system and trains T-cells what to do and where to go. The innate immune system, like the adaptive immune system, contains checkpoints that regulate the immune response. Drs. Rothlin and Ghosh think these checkpoints can be manipulated to stimulate a greater array of T-cells into hyperactivity and thus boost the overall immune response to cancer, irrespective of a tumor’s type or location.

It’s often said that immunotherapy “takes the brakes off of T-cells.” Dr. Rothlin uses a different image to illustrate what she and Dr. Ghosh have in mind. “Imagine that the anti-tumor response is an army,” she said. “Your T-cells are the soldiers at the site of the battle, the tumor. But the soldiers are tired or don’t have weapons. Current immunotherapies make the soldiers better. But what if you don’t have any soldiers at the battle site? That is, some tumors don’t have T-cells, so there are no soldiers to be activated by current immunotherapies. ’So we go further upstream,’ continued Dr. Rothlin, ’to your innate immune response, the ultimate command center—the innate immune system. It’s older and more primitive, and it’s primary. It activates the adaptive immune system and trains T-cells what to do and where to go. The innate immune system, like the adaptive immune system, contains checkpoints that regulate the immune response. Drs. Rothlin and Ghosh think these checkpoints can be manipulated to stimulate a greater array of T-cells into hyperactivity and thus boost the overall immune response to cancer, irrespective of a tumor’s type or location.”
which makes sure that soldiers get the right instructions and the right weapons and are transported to the right place to kill the cancer cells."

"The innate immune cells train the T-cells," added Dr. Ghosh. "We are trying to make the trainers better. One way we do that is that there are molecules in the trainers that are brakes, and some of these molecules are receptor tyrosine kinases. We can generate small molecule inhibitors or even use biologics to inhibit the inhibitors to break the brakes. That makes the trainers hyperactive, so they train the T-cells better to get to the site of the tumor."

If T-cells could be sent into the large group of tumors that lack them, the effect would be profound. Tumors without T-cells cannot mount an immune response and are not affected by immunotherapies that depend on T-cells. Such tumors can be referred to as "cold" compared to "hot" tumors with active T-cells. Drs. Rothlin and Ghosh are comparing cold and hot tumors, looking for mechanisms and pathways in the innate immune system that can be manipulated to direct T-cells to where they are needed, making cold tumors hot with cancer-fighters."

"That's a big need that we need to fill," explained Dr. Ghosh. Their research focused on a group of receptor tyrosine kinases called TAMs (TYRO3, AXL, and MERTK) that help regulate the immune system's response to inflammation. TAMs gradually decrease the inflammatory response and assist in tissue repair."That's important when you want to survive an infection," said Dr. Rothlin, "but it turns out that in cancer, this resolution also turns off the immune response. But if you inhibit the TAMs, you release the brake of the innate immune response and mount a much stronger response to the cancer."

They have also learned that some tumor cells overexpress TAMs to drive growth, so inhibiting them might also damage the tumors themselves. "That's almost a bonus," said Dr. Ghosh, "because you are simultaneously boost the immune response and also target the tumor. But our focus is the immune system because that's more widely applicable."

Another bonus, he continued, is that going upstream to the adaptive immune system offers access to cell types that don't occur in the adaptive immune system, such as natural killer cells. The scientists are currently studying this in mouse models. Once they are satisfied with their understanding of the basic biology, they will hand off their findings to drug developers who can design the inhibitors.

They hope that the result of their work will be immunotherapies that are more powerful, sustained, effective, and broadly applicable. "We are super excited," said Dr. Ghosh. "We are attacking cancer in many ways, not just with one weapon or one target."

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Dr. Ranjit S. Bindra, MD, PhD, Associate Professor of Therapeutic Radiology and, Asher Marks, MD, Assistant Professor of Pediatrics and Director of Pediatric Neuro-Oncology, merged their strengths in the lab to create the clinical trial. “AYA cancer patients are kind of stuck in the middle,” said Dr. Marks. “Here at Smilow Cancer Hospital we have a lovely pediatric cancer clinic with clowns and toys, and then we have the adult clinic that serves mostly older patients. AYAs don’t fit into either on the psychosocial side, and they also can be different on the biological side.”

Dr. Marks points out that the National Cancer Institute devotes relatively little money to pediatric trials, and most of that goes to study young children. Pediatric trials also tend to be large phase 3 investigations at centers in major cities with access to a huge volume of patients. Further, big pharmaceutical companies are usually reluctant to fund pediatric trials because the potential market is smaller and less profitable, and the trial regulations more stringent, especially for children under 13.

“The result is that, for most drugs, the pharmacokinetics has only been studied in adults,” said Dr. Bindra. “Exactly,” said Dr. Marks. “We typically take what’s being done on the adult side and try to apply it to pediatrics. But the more we learn about the biology, the more we see that pediatric cancers have different drivers than adult cancers.”

Their new clinical trial is rooted in biological processes. Two years ago, Dr. Bindra and the scientists in his lab discovered that IDH1/2 mutations had been found in adolescent gliomas. He walked down the hall and asked if Dr. Marks would be interested in testing a new therapy for his AYA patients with brain cancer. That’s when the current trial was conceived, but much needed to be done.

“People think a clinical trial is the beginning,” said Dr. Bindra, “but it’s an enormous, complicated obstacle course to get there. There was no template for getting a rare pediatric cancer into a trial. First, we needed to show that BGB-290 was active against IDH1/2-mutant gliomas in pediatric cancer specimens. Second, we had to convince the pediatric community that these mutations were present in kids, not just adults.” Using gene sequencing data, they demonstrated that IDH1/2 mutations were indeed present in 30 to 40 percent of adolescents with gliomas. They took this data to RoGen and asked it to support an AYA trial. RoGen came on board.

Because AYA gliomas are rare, and those with IDH1/2 mutations even rarer, Yale couldn’t possibly recruit enough patients for a meaningful trial as a single center. Drs. Bindra and Marks needed a collaborating partner with lots of reach. They found one in the Pacific Pediatric Neuro-Oncology Consortium (PNOC), a network of 22 pediatric neuro-oncology centers that run clinical trials using new therapies on children and young adults with brain cancer.

The final element they needed was funding. They submitted an NIH grant, but the process can take several years. Meanwhile, young patients with gliomas need help now. Drs. Bindra and Marks applied for rapid funding from CureSearch for Children’s Cancer, which supports innovative research likely to be clinically successful. CureSearch was so impressed by Dr. Bindra’s findings that it awarded him its inaugural Culpeath Award of $1 million. Putting all these pieces together took about 10 months. The trial officially launched in April when PNOC enrolled the first patient at the University of California, San Francisco. Seventeen other institutions in PNOC’s network also are recruiting patients.

The lab worked in close collaboration with the lab of Peter M. Glazer, MD, PhD, Robert E. Hanler Professor of Therapeutic Radiology and Professor of Genetics, to test this hunch. DNA repair relies on PARP genes. When the scientists used a PARP inhibitor called olaparib to block the IDH1/2-mutant cells from fixing their damaged DNA, the results were spectacular—brain cancer cells died at 50 times the usual rate.

Dr. Bindra began looking into other PARP inhibitors that might affect IDH1/2-mutant cancers, including a newer one called BGB-290 (pamiparib), made by a Chinese company called RoGen. BGB-290 had not been tested against brain cancer at the time of their initial discovery; but after multiple phone calls and meetings, RoGen agreed to give Dr. Bindra the drug for adult trials. The results were impressive: “It’s the inhibitor with the greatest chance of getting into the brain of patients with cancer,” explained Dr. Bindra. Along the way, Dr. Bindra learned that IDH1/2 mutations had been found in adolescent gliomas. He walked down the hall and asked if Dr. Marks would be interested in testing a new therapy for his AYA patients with brain cancer. That’s when the current trial was conceived, but much needed to be done.

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Dr. Bindra and Marks, co-principal investigators, expect to enroll their first patient at Smilow this fall. The initial goal is 48 patients, with an eventual total of 68. All will be treated with a combination of BGB-290 and temozolomide, a chemotherapy. The scientists expect the trial to run for three years.

“One of the most exciting things about this, and what makes it different,” said Dr. Bindra, “is that it’s a direct translation from this bench to the clinic for pediatric patients. We’re targeting a very specific brain tumor, it is biomarker driven, and the biology suggests a novel opportunity. Regardless of what we find, we just follow the biology and this path paves the way for many more innovative, biomarker-driven trials in pediatric cancer.”
Making Cancer Part of the Conversation

Jose DeJesus was born and raised in New Haven, but that’s not why the Community Health Educator for Yale Cancer Center and Smilow Cancer Hospital is such a familiar face around town. “When I walk into stores, people say, ‘Hey! It’s the cancer guy!’” explained Mr. DeJesus. For the past four years, he has been spreading the word out to Connecticut residents about the need for cancer screening and prevention, and his message—that healthy people over 40 need to be screened for common cancers—is getting through.

“They’ll come over and ask questions about when and where the next free screenings will be held,” said Mr. DeJesus. “That’s what I’m most proud of—that we’ve become a resource for the community, and beyond.”

It wasn’t always that way. According to Mr. DeJesus, things were more difficult back in 2016, when it was just him and his supervisor, Beth Jones, PhD, MPH, Director of the Smilow Screening & Prevention Program. “When you say the word ‘cancer’, people get scared,” said Mr. DeJesus. “At first, I had to pound the pavement asking various agencies and community organizations if they were interested in having us make presentations about screening and prevention. Now, we have repeat customers. Even better, people are not just going to our free screenings once and disappearing, but they are getting screenings done at the proper intervals.”

That progress, in part, stems from Mr. DeJesus’s natural enthusiasm—he is a man on a mission, determined to target people who might not otherwise think about mammograms or skin checks on a regular basis. He understands the obstacles that some of Connecticut’s neediest residents face, from homelessness to food insecurity to addiction issues. “If I was a homeless person, I wouldn’t want to bother with screenings either. But you have to be respectful, and to meet people where they are.”

Besides mammography, Mr. DeJesus and the community outreach team—which is now seven people strong—offers talks and free screenings for lung, prostate, colorectal, breast, cervical, skin, and head and neck cancers. “All the departments [at Yale] are working together to help reduce disparities in cancer outcomes among different populations across the state,” said Mr. DeJesus. “If we do our job right, then everyone will be screened, and if they have cancer, we’ll catch it early when it can be cured.”

Mr. DeJesus and the screening team are well on their way to that goal. In 2016, the program’s first year, they sponsored 24 community outreach events in Connecticut that reached 2,205 people. In 2019, there were over 100 community outreach and education events that reached 6,543 individuals, whether in Torrington, where Mr. DeJesus brings a pair of giant inflatable lungs to presentations to help combat higher rates of smoking and lung cancer; or in Hartford, where they target the large Latino population for prostate cancer screenings. “The rate of prostate cancer is five times higher in Latino men,” said Mr. DeJesus. All told, the program has delivered small group education sessions or free screenings to a whopping 18,467 people, quadruple the number in 2016.

There’s a real need for this kind of “boots on the ground outreach,” as Mr. DeJesus calls it. “Connecticut is in the highest quartile for cancer in the United States—particularly breast cancer and prostate cancer,” said Dr. Jones. She also points to the state’s history of ‘residential segregation,’ in which poorer residents who are less likely to be screened tend to be concentrated in urban areas. “That’s why we are reaching beyond New Haven to focus on other urban pockets across the state.”

Along with that, the team is considering various social and economic factors that might make it difficult for people to get to the doctor and enrolling vulnerable residents in its new health navigation program, which goes beyond screenings to try to address problems like housing insecurity, addiction issues, mental health problems, and more. “It’s one thing to go into the community and give people information, but we are also taking the extra step to help people get tobacco treatment, or steer them to places where they can exercise, or access healthier food,” said Dr. Jones.

Sometimes, the obstacles to health can be more basic, like difficulty scheduling a screening appointment. “Often, people don’t know who to call to get a colonoscopy, or they give up when no one calls back,” explained Monique Stefanou, a Community Health Educator and the team’s lead Health Navigator. “I answer calls from our information line and set up appointments,” she said. “One woman went to our skin cancer screening in Trumbull, and the doctor found something that had to be removed. Later, she called, and said, ‘Do you have any other screenings coming up?’ I love getting people connected to care.”

Another new initiative: Starting in 2020, the team will be providing FIT kits to Connecticut residents to encourage them to do a self-screening for colorectal cancer, which is on the rise, particularly among younger people. The at-home tests detect whether blood is present in stool. “We’ll do follow up calls, and if someone’s test comes back positive, they’ll move to the front of the line for a colonoscopy,” said Mr. DeJesus.

Some people might be squeamish talking to strangers about colon cancer or stool tests. But Mr. DeJesus relishes the challenge. “I love my job—in fact, I don’t even consider it a job. I’m not selling anything; I just want to give out information on screenings, and help people to those appointments. I tell my boss all the time—it feels amazing.”

All the departments [at Yale] are working together to help reduce disparities in cancer outcomes among different populations across the state. If we do our job right, then everyone will be screened, and if they have cancer, we’ll catch it early when it can be cured.
I've been so pleased to be a part of a place where the growth of advanced technologies in cancer control is a priority. It has been rewarding to see so many developments over the past 20 years; I know we'll see even more of them in the years ahead.

Mr. Kelly appreciated his high caliber of care and was impressed by the advances in cancer treatment being pioneered locally at Yale. He wanted to support Yale Cancer Center philanthropically—and the Director's Advisory Board provided the perfect opportunity to do so. "I've been so pleased to be part of a place where the growth of advanced technologies in cancer control is a priority," he said. "It has been rewarding to see so many developments over the past 20 years, I know we'll see even more of them in the years ahead."

Mr. Kelly and his fellow members of Yale Cancer Center's Director's Advisory Board support the Center's initiatives in a number of ways. "The board acts as a sounding board for the director," explained Julie Parr, Yale Cancer Center's Senior Director of Development. "They also are ambassadors to external constituents. They lead the philanthropic charge of the Cancer Center. They help make connections to people who might be interested in the Center and they prioritize Yale Cancer Center philanthropically."

Mr. Kelly directs his significant annual contributions to the Yale Cancer Center Director's Fund, a crucial source of funding for the Center's top priorities. "The fund enables the director to respond to the most urgent needs of the Center," Mr. Parr explained. "Dr. Fuchs can direct attention and resources to unique or new research projects that show tremendous promise."

"Through the generous and gracious support of Paul Kelly and others, Yale Cancer Center is able to remain at the forefront of cancer care and research," said Charles S. Fuchs, MD, MPH, Director of Yale Cancer Center and Physician-in-Chief of Smilow Cancer Hospital. "His generous commitment to Yale Cancer Center's Director's Fund is a profound expression of his loyalty and confidence in our work."

During Mr. Kelly's tenure, the board served a critical role in raising the funds needed to build the state-of-the-art Smilow Cancer Hospital. The 14-story, 500,000-square-foot facility has now been serving patients for a decade. With the board's support, Yale Cancer Center also was able to expand to West Campus, launch the Cancer Biology Institute, and open new Smilow Cancer Hospital Care Centers across the state.

"Drawing on his decades of business expertise, Mr. Kelly sees the clinical expansion as crucial to helping Yale Cancer Center and Smilow Cancer Hospital stay ahead of the curve. "You see smaller organizations affiliating with leading hospitals from out of state," he said. "Such branding can give you a business a big boost. Yale is really the only hometown game in this market. By expanding our facilities and opening clinics around the region, you're solidifying Yale's standing in Connecticut and providing the best care available to the people who need it."

Mr. Kelly himself connected a person desperately in need of care with Smilow Cancer Hospital's cutting-edge treatments. One day a friend told him about an acquaintance in her forties who had developed a rare form of cancer and was given six weeks to live. The description of her condition reminded Mr. Kelly of something he had heard at a recent board meeting—the hiring of a new researcher whose hiring the board had thought to be insurmountable," Mr. Kelly explained. "I think about how many other people are in that situation, of possibly being able to overcome something thought to be insurmountable," Mr. Kelly said. "It adds to the call, the feeling that you want to be a part of this. Yale Cancer Center does exceedingly good work, and I'm very grateful to have the opportunity to be a part of what they are accomplishing."
January-June 2019

Katerina Politi, PhD, received funding of a Research Project Grant from the National Institutes of Health (NIH) for her project, “Understanding and Overcoming Resistance to Cancer Immunotherapy Due to Defective Antigen Presentation.” Co-investigators include Peter Cresswell, Paula Kershaw, Rong Fan, Kurt Schubert, as well as Roy Herbst, Scott Gettinger, Marcus Rosenberg, Aaron Ring, and Nikhil Joshi at Yale and Lewis Larue at UCSF.

Nadine Houri, MD, and Sanjay Anjua, MD, were awarded a National Science Foundation grant to use theMednet to build machine learning technology to raise physician awareness of clinical trials.

Susan Baserga, MD, PhD, was awarded a 2019 Breast Cancer Alliance Exceptional Project Grant to support her research project, “Targeting the Nucleolus for Breast Cancer Therapy.”

Michael Leapman, MD, was awarded a K08 Clinical Investigator Award from the NIH to support his project, “Understanding the Adoption and Impact of New Risk Assessment Technologies in Prostate Cancer Care.”

The International Cytokine & Interferon Society announced that the Seymour & Vivian Milstein Award has been bestowed on two world leaders in deciphering the fundamental mechanisms of innate immunity in directing cytokine-driven responses. Yale Cancer Center’s Akiko Iwasaki, PhD, shares the award with Hao Wu, PhD.

Don Nguyen, PhD, and Katerina Politi, PhD, received a 5-year National Cancer Institute (NCI) grant to support, “Uncovering the Biology of Resistance to Tyrosine Kinase Inhibitors in EGFR-Mutant Lung Cancer Patient Derived Models.”

Mandar Murumdar, MD, received the Cancer Research Early Career Award from the American Association for Cancer Research, recognizing outstanding early career investigators who have authored peer-reviewed, original articles published in Cancer Research that have made a significant impact in one or more of the fields represented by the Journal. Dr. Murumdar was honored for his publication, “Adaptive and Reversible Resistance to Kras Inhibition in Pancreatic Cancer Cells.”

Craig Crews, PhD, was awarded the 2019 Pharmacology-ASPET Award for Experimental Therapeutics from the American Society for Pharmacology and Experimental Therapeutics (ASPET).

Liping Chen, MD, PhD, gave the Society of Surgical Oncology’s 2019 James Ewing Lecture on “Immunological Principles of Anti-PD-1/PD-1L Cancer Therapy.” The James Ewing Lecture is the highest award of the Society, given to a physician whose work has had a major impact on surgical oncology.

Yuvul Klinger, PhD, received a Research Project Grant from the NHR to support his project, “Efficient Methods for Calibration, Clustering, Visualization and Imputation of Large scRNA-Seq Data.”

Nikhil Joshi, PhD, was awarded the Distinguished Young Investigator Research Award at the 16th Annual Immunology Young Investigators’ Forum for his abstract, “Engineering NJINJA for Studies of Cancer Immunosurveillance.”

Xiaolei Su, PhD, received a Child Health Research Grant from the Charles H. Hood Foundation to support his research into the Mechanism of Chimeric Antigen Receptor (CAR) Signaling.

Noah Palm, PhD, was named a 2019 Pew Scholar in the Biomedical Sciences.

Yale Radiation Oncology received full accreditation from the American Society for Radiation Oncology (ASTRO) Accreditation Program for Excellence (APEX) for four years.

Deborah Blythe Doverhoff, MD, PhD, was awarded the Journal of Clinical Oncology Young Investigator Award from the Conquer Cancer Foundation to support her work, “Targeting DNA Damage Repair Mechanisms in IDH1/2 Mutated Intrahepatic Cholangiocarcinomas and Other Solid Tumors.”

Peter Tattersall, PhD, received a two year R21 grant from the National Cancer Institute to pursue studies on Armed Oncolytic Parovirus Vectors for Modulating the Tumor Microenvironment.

Roy S. Herbst, MD, PhD, was named to the Board of Directors for the International Association for the Study of Lung Cancer (IASLC).

Ranjit Bindu, MD, PhD, received a grant from the Rising Tide Foundation to support funding for biomarkers for their phase I clinical trial testing olaparib against IDH1/2-mutant cancers.

Genosity

January-June 2019

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The Breast Cancer Research Foundation
The Frederick A. DeLuca Foundation
The Gray Foundation
Howard Hughes Medical Institute
The Sherwin B. Neilan Foundation
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Pink Aid, Inc.
Mr. George Schussel
and Mrs. Sandra Schussel
Mr. and Mrs. Alan G. Weiler

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Big Y Foods, Inc.
Bottle It Up
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Connecticut Brain Tumor Alliance Inc.
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Mr. Spyros Niarchos
North Texas Community Foundation
Mr. David Park
Mary-Lake Polen, MD, PhD,
and Frank A. Remack, Jr.
Mrs. Carol V.C. Schaller
Schwab Charitable Fund
Mr. and Mrs. Roger Vassey
Mrs. Elizabeth N. Welke
Smilow Cancer Hospital Care Center at North Haven

The Smilow Cancer Hospital Care Center in North Haven is newly renovated and provides our patients with a beautiful and easy to access location for their cancer care. We coordinate with our colleagues on our main campus in New Haven to ensure all treatment options are reviewed through comprehensive tumor board meetings, and the best care is provided to each patient.

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Neal Fischbach, MD
Assistant Professor of Clinical Medicine (Medical Oncology)
Assistant Director of Clinical Research, Care Centers

You have focused your delivery of cancer care in our community through the Smilow Cancer Hospital Care Center Network. How does the Network collaborate with our academic center, while providing our patients community-based cancer care?

Our Care Center model allows me to provide care for our patients where we live while leveraging all the resources of Smilow Cancer Hospital. Our pathology is performed by world-class, organ-specific Yale Pathologists, giving me 100% confidence in our initial diagnosis, the critical first step in therapy. Cancer care is increasingly multidisciplinary and we have a tremendous network of organ-specific Yale Pathologists, Radiation Oncologists, Pathologists, Radiologists, and Genetic Counselors. We are also able to touch the lives of people living with cancer in very tangible and profound ways through our Social Work staff, providing assistance with medication co-pays, coordinating financial assistance with bills, and offering counseling. The breadth and depth of our supportive services are unparalleled. Lastly, our integral involvement in the academic mission of Yale Cancer Center allows us to actively participate in shaping the future of cancer care through clinical trials and practice quality improvement, an engagement which ensures we’re offering those we care for the very latest and most thoughtful interventions.

Our ability to offer clinical trials to patients in the community settings through our 14 care centers has greatly expanded over the last several years. Where do you see the expansion continuing?

Through the ground breaking efforts of my colleagues, most recently Dr. Kert Sabbath, we have built an extraordinary clinical trials network. We live by the mantra that the best cancer care includes the opportunity to participate in clinical trials at all phases of disease. We are continuously striving to expand our portfolio of trials to include all cancer types and across the continuum from cancer prevention, diagnosis and staging, reducing recurrence after curative surgery, and all lines of metastatic disease. We’re exploring new ways to identify people who may be candidates for clinical trials. We are also working to improve our participation in the earliest phases of clinical trial design and translational research by providing samples of tumor tissue, which are essential to identifying new targets for therapy.

Your focus on care of patients with breast cancer allows for collaboration with surgeons and radiation oncology in Trumbull. How does the multidisciplinary team unite to benefit your patients?

As I previously mentioned, cancer care is increasingly multidisciplinary and requires close communication between a diverse team of providers. Nowhere is this more evident than breast cancer. Our Multidisciplinary Breast Tumor Board includes Yale Breast Surgeons, Medical Oncologists, Radiation Oncologists, Pathologists, Radiologists, and Genetic Counselors. Our Multidisciplinary Breast Tumor Board allows for collaborative care for patients in the community settings.

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Read their stories:
yalecancercenter.org/survivors