





The 70-year -old retiree from South Bend, Indiana, couldn't pinpoint anything specifically wrong, except for a persistent cough. The nurse practitioner at her doctor's office told her that it was probably viral, so Butkera didn't worry. But after about a month, her regular physician suggested getting an X-ray of her lungs.

"I said, 'Wait, do you think I have lung cancer? Is this a joke?" she remembers. "But he said, 'Better safe than sorry."

When she got home later that afternoon, her husband, Eddie, met her in the kitchen. With a stunned look, he told Butkera that her doctor had called to say that there was a mass on her lung. A biopsy soon afterward confirmed that it was cancer.

Although more than 234,000 people are diagnosed with lung cancer each year in the U.S.—making this the second most common cancer in both men and women—they don't all receive the same model of care. At most hospitals around the country, diagnosis and treatment revolve around the care team, with a series of visits with medical, surgical and radiation oncologists and other specialists at different locations. Numerous appointments for tests, care decisions and treatments are spread out over time. However, at the Kimmel Cancer Center's Thoracic Oncology Multidisciplinary Clinic on

the Johns Hopkins Bayview campus—where Butkera receives her care—providers follow an opposing model in which the care team revolves around the patient in one central location.

This new model hasn't just eased the lung cancer journey for Butkera and other patients—studies show that it is also lengthening lives while cutting health care costs.

#### Building a Better Clinic

Radiation oncologist Russell Hales, director of the Thoracic Oncology Multidisciplinary Program, based at the Kimmel Cancer Center on the Johns Hopkins Bayview campus, says that he got the idea to start the clinic in 2011, during his first year at the Kimmel Cancer Center.

As a downstream provider who typically sees patients after they've already seen several other members of the care team, he'd often meet patients at the peak of frustration and stress. Many had already been through numerous appointments to see other specialists one by one over the course of months, with a bevy of diagnostic tests done on different days. Information about their condition was doled out piecemeal as each test was completed. Providers sometimes gave conflicting information or repeated

the same test because of a lack of communication. Even paying for parking repeatedly added to the hassle.

"I'd look into the eyes of these patients and see people who were scared to death about their cancer diagnosis and worried that we were extending this worry with each additional appointment," he remembers. "Our approach is to take all those different appointments and bottle them up into a single clinic visit."

To make that idea a reality, Hales and his colleagues in thoracic oncology needed to design a completely new kind of cancer treatment space.

Rather than having medical, surgical and radiation oncologists in three different locations, they were co-located at the same site. Their nurses—along with the technicians who perform imaging and other diagnostic tests and all their equipment—also needed to share the same setting.

Additionally, Hales says, at Johns Hopkins, much like most large hospitals, funds run through separate departments. To make a shared space like he'd envisioned, several departments needed to pool their resources—a mundane but consequential undertaking.

After years of planning, Hales and colleagues who had been scattered across The Johns Hopkins Hospital campus moved into their new combined space on the Johns Hopkins Baview campus in 2015. It was just in time for Butkera's first appointment in December of that year.

#### A Patient Guide

After Butkera recovered from the initial shock of her diagnosis, she called each of her children to let them know what was happening—including her daughter, Jessica, an attorney who lives in Baltimore and has worked with Johns Hopkins. Jessica and her friends helped Butkera connect with Peggy Lang, a nurse practitioner and Thoracic Oncology Multidiscipinary Clinic coordinator.

"I talked with Peggy on a Tuesday, and she asked how soon we could get there," Butkera remembers. "We were in the car on Wednesday."

Lang is usually the first contact that patients make at the clinic, and



her work starts before patients ever arrive. She gathers all necessary records from other providers and determines and schedules tests and imaging patients still need.

The clinic offers initial visits for new patients once a week, starting at 9 a.m. When patients first arrive, they meet with a resident, fellow or another nurse practitioner to take a detailed history and perform a physical exam, a process that takes about an hour. Then, around 10 a.m., Lang leads an educational session for patients and whoever came with them—often a spouse or an adult child.

Butkera had both Eddie and Jessica with her on that first clinic day. She remembers feeling numb as Lang gave her and five other patients a two-hour tutorial on what they'd need to know about lung cancer, including risk factors for the disease, how staging works, how cancer can spread from its primary site, how different treatments work and why nutrition is important, among other topics.

Patients are given a lot of information, says Lang, but many find it empowering. "The more they know, the less there is to fear. There's also camaraderie in meeting other patients with the same diagnosis," she says. "I like to think that I'm making a very difficult situation better. Many times, patients just need someone to talk to, someone to explain it, and they need to hear it with compassion and understanding."





#### All in a Day's Work

After the education session, all the patients head to lunch together as a group — an opportunity for them to get to know each other better and make contacts for support—while the care team leaps into action at the clinic. After spending time reviewing each patient's chart beforehand, they'll spend the next hour deciding on the best care to recommend to each patient, explains Josephine "Joy" Feliciano, medical director of the Thoracic Oncology Program.

It's a meeting akin to the tumor boards that many cancer centers hold usually once a week, in which every member of the care team—doctors, nurses and other care providers involved in the treatment—discuss every aspect of each patient's condition to come up with a plan. Rather than talk about patients who visited days ago—the practice at many other cancer centers—Kimmel Cancer Center experts discuss the patients seen at the clinic that same day.

"We're not just discussing the treatments that they'll need for that stage of cancer, but what other resources we'll need to enlist for each patient based on what we know about them—their medical history, social history, their life circumstances—because treatment isn't just about the cancer itself," Feliciano says. "It's about how this patient might need rides to chemo or that one might need us to



coordinate care with their cardiologist because they have a pacemaker."

Once the doctors conclude their meeting, it's time to meet with patients. Medical oncologists, surgical oncologists and radiation oncologists, or any combination of these three, see each patient and discuss their recommendations for the next steps.

This single-day approach is highly unusual in cancer care, explains Hales, where patients generally have to visit doctors at different sites. All the aspects of this first clinic visit—including the exam, education session, lunch and tumor board meeting—unquestionably make for a long day.

"But patients get to leave in a day with a plan that would have taken weeks to develop elsewhere," says Hales. "We pride ourselves on that long day because so much gets accomplished."

#### All the Experts Together

Tests revealed that Butkera's tumor was situated in a way that would make surgery challenging. The cancer had also spread to tissue near her hip. She and her husband nicknamed it "the floater." Her care team recommended combined therapy with chemotherapy and radiation. Soon after that initial appointment, she started treatment.

Thoracic surgeons are prepared for challenging scenarios like Butkera's. "A high proportion of our patients receive treatment before surgery, but our

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outcomes are as good as everywhere else, despite the complexity," says Richard Battafarano, director of general thoracic surgery and a member of the multidisciplinary team.

After the initial diagnosis and planning, treatments and follow-up appointments also continue at the Kimmel Cancer Center on the Johns Hopkins Bayview campus. Having all the experts together helps facilitate treatment discussions, explains Hales. "If a scan reveals that a patient's cancer has returned, I can consult with my colleagues in medical oncology to discuss starting chemotherapy right away, as opposed to waiting a week or longer to get a new appointment on the books," he says. Working in the same physical space also influences clinician-scientists' research programs, spurring new questions and plans for studies.

"It allows each member of the care team to work together more seamlessly," says nurse Ramsey Valenti, who works with Hales. Although specialties may vary among nurses, she says, "we're all in two-second walking distance to each other." That close proximity helps them learn more about each patient-such as which days each patient needs chemotherapy or bloodwork, or which ones are candidates for surgery and need follow-up-allowing them to deliver unified information to patients and work together to improve care.

Patients also appreciate the short distance from one treatment area to the other, Hales adds. "If patients are getting chemotherapy and radiation on the same day, they'll walk 200 feet from one area to the next, instead of from one building to the next."

#### The Proof

Although Hales and colleagues knew this new model worked for Kimmel Cancer Center patients, they wanted objective data that provided evidence for other medical institutions to show this model was an investment worth making. He and his colleagues put the clinic to the test to quantify the increased value for patients and the health care system.

"Value is a buzzword in medicine these days, and increasing value can

















mean one of two things—improving care at the same cost or reducing cost for the same level of care," he says.

Two years ago, Hales and colleagues presented data at the American Society of Radiation Oncology (ASTRO) meeting, comparing the outcomes of lung cancer patients who received care through the multidisciplinary clinic with patients who received their care outside of the clinic-either in the years just before the clinic opened or with individual providers through a more traditional care model. Their findings showed that one-year survival at the clinic was 82 percent, compared with 64 percent for patients treated outside the clinic.

Last year, Johns Hopkins radiation oncologist Ranh Voong presented additional data at the ASTRO meeting, showing that the clinic provides a cost savings of 30 percent over traditional care—presumably because patients receive more streamlined planning and treatment, avoiding unnecessary appointments and tests.

"You don't see this magnitude of improvement in some of the newer drugs coming out, and it's even more significant because patients and the health care system are saving money," says Hales.

Butkera says her treatment has involved several twists and turns. She's had two courses of chemotherapy and radiation over the past three years, and she returns to the Kimmel Cancer Center for follow-up care to receive new scans every three months. In the meantime, she's seen her daughter get married, watched her grandchildren grow and celebrated her 48th wedding anniversary—none of which she believes would be possible without the care she's received.

"I can't say enough about the doctors, nurses, technicians and everyone at the clinic," she says.

"They've made a really bad, scary situation much more bearable."

#### WEB EXCLUSIVE:

Lung Cancer Surgery with Dr. Benjamin Levy and Dr. Stephen Broderick: http://bit.ly/2CmDYke





#### SPECIALTY CARE

#### **Expert Surgeons**

At Johns Hopkins and other medical centers across the country, outcomes from lung cancer surgeries are getting better and better, say thoracic surgeons Stephen Broderick and Richard Battafarano. That's largely due to changing philosophies and approaches, they add. For example, about 75 percent of surgeries for earlystage lung cancer now take place in a minimally invasive fashion.

"We don't hesitate to use an open approach when necessary," says Broderick. "But when possible, a minimally invasive approach leads to less pain, a shorter length of stay and improved outcomes."

In the Kimmel Cancer Center, Broderick, Battafarano and thoracic surgeons Errol Bush, Malcolm Brock, Jinny Ha and Stephen Yang are developing better techniques, such as operations after patients have already been pretreated with chemotherapy or immunotherapy, to advance therapy and improve outcomes for the most complicated cases.

#### Interventional Pulmonology

Interventional pulmonology is a relatively new subspeciality of pulmonary medicine. But it's already making huge strides in diagnosing patients earlier and

boosting survival, say Johns Hopkins

interventional pulmonologists Lonny Yarmus,

David Feller-Kopman, Hans Lee and Andrew

Lerner. Each of these specialists is helping to



Yarmus, D.O.

develop new technology or protocols that continue to improve patient care. For example, Yarmus is currently the principal investigator for two clinical studies. One is a

multicenter prospective clinical trial that's investigating electromagnetic navigation—a type of GPS for the lungs—to help locate small nodules for biopsy. Another trial is helping to develop a hand-held device that analyzes a patient's breath for lung cancer biomarkers. A third trial, led by Lee, is combining bronchoscopy with genetic

information from patients to stratify the cancer risk of lung nodules.

"Each of these efforts is aimed at earlier identification, earlier diagnosis and earlier treatment, which lead to higher survival," Yarmus says.

Johns Hopkins is also one of the top centers for endobronchial ultrasound. helping develop consensus statements that are guiding the field, adds Feller-Kopman. "It's not a rare technique anymore, but performing it well is very important," he says. "We have long been leaders in this area."

"Every year, there are newer and newer techniques and technology," adds Lerner. "Each advance is helping us provide even better care for our patients."

#### **Locations in the National Capital Region**

Over the past decade, the Kimmel Cancer Center has grown, with locations now in the national capital region at Sibley Memorial Hospital and Suburban Hospital. Despite this growth, our experts remain committed to maintaining the team



approach, says lung cancer expert Benjamin Levy, clinical director of medical oncology at Sibley. Radiation oncologists Jean Wright, who directs the Breast Cancer Program and treats thoracic malignancies at the Kimmel Cancer Center at Siblev, and Stephen Greco, who directs the Department of Radiation Oncology at Suburban

Hospital, say they meet twice a week.

Wright and Greco join colleagues based at the Johns Hopkins Bayview and East Baltimore locations for tumor boards, using video conferencing technology. The groups discuss the best care for patients. "We've developed a more unified approach across these different sites," says Greco. For example, interventional pulmonologist Andrew Lerner, who performs procedures at Sibley, attends Suburban's tumor boards to share his expertise on diagnosis, staging and treatments.

"We now have a full multidisciplinary team so we can offer our patients the best care, regardless of location," says Wright.

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#### [Profile]



## Lessons from Two Battlefields

#### A Military Hero Confronts Advanced Lung Cancer

U.S. Army Special Forces veteran Ronald Shurer is no stranger to tough battles. The Green Beret and senior medic was awarded the Medal of Honor in 2018—the country's highest military honor—for fighting for more than an hour to reach and care for members of his unit when attacked by 200 enemy fighters during the Battle of Shok Valley in Afghanistan on April 6, 2008.

In March 2017, Shurer unexpectedly found himself on a new kind of battlefield, facing a sneak attack by a different kind of enemy—lung cancer.

The battle is longer and the methods different, but the strategy is

a bit similar, as 40-year-old Shurer works with his Johns Hopkins Kimmel Cancer Center oncologist **Ben Levy** to monitor the enemy and adjust the attack to defeat as many of the invading cancer cells as possible.

"In a lot of respects, I'm approaching cancer in the same way I approached my Army missions, relying on gains and surrounding myself with great people," says Shurer.

He was diagnosed two years ago after ongoing hip and back pain turned out to be spreading cancer.

After leaving the Army in 2009, Shurer became a member of the Secret Service, a job that often required carrying heavy gear.

"I distinctly remember hiking through Yosemite National Park with the Obama family and my back seized up a lot," says Shurer, who was with the former first family as part of its Secret Service detail.

He was carrying a lot of gear, and this combined with the physical demands of his years of military service seemed to point to some type of muscular injury. It made sense to Shurer, and for a time, he got some relief with chiropractic care. Unfortunately, the pain remained and worsened over time.

Imaging to explore his escalating hip pain revealed a fracture, but the worst news came when additional imaging revealed the fracture was caused by cancer that had spread throughout his body.

The diagnosis was the most advanced stage of adenocarcinoma of the lung, a type of non-small cell lung

cancer, which typically develops in the bronchioles—the small, branchlike airways in the lungs. When the medical director for the Secret Service, a former Johns Hopkins doctor, learned of the diagnosis, he sent Shurer to the Johns Hopkins Kimmel Cancer Center.

Shurer opted for treatment at the Kimmel Cancer Center's Sibley Memorial Hospital location in Washington, D.C., as it was closest to where he lived and worked, under the care of Levy, a thoracic cancer expert and clinical director of medical oncology.

The lung cancer had already spread, so surgery was not a treatment option, but Levy gave Shurer hope from the onset. "Dr. Levy said, 'We have good treatments. There are things we can do,' and that was huge. I felt like we could put up a fight," says Shurer.

Among the first things Levy did was order genetic testing of Shurer's cancer and found it was among the 15 to 20 percent or so of non-small cell lung cancers that contain mutations in a gene known as EGFR. Although, the gene alteration actually fuels the growth of the cancer, it is also a target for treatments with drugs that slow or stop the cancer by blocking the gene.

The gene mutations that support cancer growth and spread can also be its Achilles' heel. Drugs that interfere with the genes are called targeted therapies and are a promising and relatively new kind of cancer therapy. Unlike standard chemotherapy, which directly but somewhat indiscriminately kills rapidly dividing cells-cancer cells and normal cellstargeted therapies work by interfering with an unchecked mechanism that fuels the cancer to start, grow and spread. Shutting down that mechanism can slow or stop the growth and spread of cancer cells. Of course, targeted therapies only work if the cancer has the target, and for Shurer, that was the case.

He was treated with an EFGRblocking drug called afatinib—one pill taken orally every day—and for almost two years, it kept his cancer in check. Radiation oncologist Jean Wright also treated some of Shurer's tumors with radiation therapy to alleviate pain caused by the cancer.

In March 2017, on a scale of 1 to 10, Shurer classified his pain as a 9. "After three weeks of radiation with Dr. Wright, it was a 3," he says.

Levy understands advanced cancer and how it can turn the tables



to become resistant to treatment, so he was always developing multiple plans to go after Shurer's cancer. With advanced cancers like Shurer's, it's unlikely that treatment will make him cancer-free, but they can hold the cancer in check, keeping it from growing, essentially converting it to a chronic state that patients can live with.

"Even when things were going great, he was always looking for ways to improve our position or to shift course if things started going the other way," says Shurer.

That was the case in October 2018, just a few weeks after his Medal of Honor ceremony, when a CT scan revealed the cancer was growing again. The first EGFR inhibitor knocked the cancer back quite a bit and held it in check for 19 months, so Levy plans to use a newer and better iteration of the drug to stabilize Shurer's cancer once again. If newer versions of the drug don't work, he has several other treatment options he is considering, including the possibility of a clinical trial. He had Shurer's cancer studied again to identify any new mutations that might be amenable to other targeted therapies.

"Of course, I'm not excited that the cancer is progressing again, but I don't have any question that Dr. Levy has three, four or five plans ready to go," says Shurer. "If the first one doesn't work, he'll move to the next one." There are currently four EGFR inhibitors that are FDA approved for advanced lung cancers like Shurer's. There are also other gene mutations that respond to targeted therapies.

"New gene mutations that cancers acquire over time, called resistant mutations, may make targeted therapies stop working, but fortunately, have led to the development of next-generation targeted therapies that may be effective," says Levy. "While historically, immunotherapy, like checkpoint inhibitors, has not worked in most patients with EGFR mutations, ongoing clinical trials are evaluating newer immunotherapeutic approaches that are promising. Other drugs, called antiangiogenesis agents, that cut off the blood supply that nourishes tumors also work against some lung adenocarcinomas, including EGFR mutation patients."

Cancer seems an unthinkably cruel reality for someone who has already sacrificed so much. Still, the husband and father of two young boys remains fixed on the future. In those inevitable moments of despair, he credits his wife, friends and medical team for helping to keep him positive, focused and determined.

Special Forces military training helps. "You don't get a Medal of Honor because things went well for you that day," says Shurer. He says facing adversity and life and death in his military service helped prepare him emotionally for his cancer battle.

"When I was overseas, I saw how life could just be taken away in the blink of an eye. I have friends who didn't come home. I've had to fight cancer for the last two years, but I'm still with my family. I'm still enjoying things. I'm thankful for that," Shurer says.

He remains confident in the expertise of Levy, Wright, nurse practitioner Rasheda Persinger and all of the Kimmel Cancer Center at Sibley experts who provide his cancer care.

"They take great care of us every time we're there. They listen to us, and we appreciate that," says Shurer. "They have our complete trust. We are in this fight together."

### Breaking Down Barriers to Lung Cancer Treatment



Differences in the health status of various groups of people are known as health disparities, and they are becoming a focus of attention among health care providers. Factors such as race, ethnicity, immigrant status, disability, sex or gender, sexual orientation, geography and income can all impact how illness and disease affects someone.

Like many illnesses, lung cancer does not discriminate. It is known to disproportionately affect specific populations, with differences in the incidence, treatments, and outcomes, such as survival. For example, the American Cancer Society reports that black men are at roughly 20 percent higher risk of lung cancer than white men—even if they don't smoke.

Through various clinical and academic research efforts, pilot projects, and support from the Wayne K. Curry Lung Cancer Disparity Awareness Fund and P.J. Aldridge Foundation, Joy Feliciano, Johns Hopkins Kimmel Cancer Center lung cancer expert, is working to break down the barriers within populations who experience health disparities.

#### Access to Care and Care Delivery

All along the way, these patients face hurdles to optimal care for their disease. The problem starts even before they are diagnosed, with a lack of access to primary care physicians or not being under the care of a primary care physician. These doctors are very important because they are often the clinicians who first suspect the presence of cancer.

"People may not have primary care physicians to whom they can bring their complaint or who is moni-



toring them regularly," Feliciano says.
"If not, they may not be undergoing routine screening for lung cancer or may not be evaluated early enough, when they start to have symptoms."

People who lack access to primary care are also unlikely to undergo screening for lung cancer, even if their risk for developing the disease is elevated—if they smoke, for example, or have been exposed to certain chemicals in the workplace.

Taken together, these factors add up, resulting in patients who are less likely to receive stage-appropriate evaluation and therapy. Feliciano is working to improve the delivery of cancer care throughout the whole timeline of the disease.

#### Representation in Clinical Trials

African Americans and other underserved and minority populations are underrepresented in clinical trials of new treatments. Working with patient navigators, Feliciano hopes to identify more patients with lung cancer in the area who are eligible for studies but may be unaware of the promising new treatment options being studied. She also is collaborating with **Dina Lansey**, assistant director of diversity and inclusion in clinical research, to see if her patients can be included in a study

to determine if providing free transportation or parking has a positive impact on clinical trial participation.

#### Lack of Social Support and Access to Resources

"Something that can make a huge impact for these patients is having support from social workers and counselors," says Feliciano. "It's not just the cancer they're dealing with. It's many issues at home. Lung cancer is really a disease that affects the whole family at many levels. There is a lot of room for improvement for resources to be directed to those who need them most."

Feliciano works with social workers and navigators to make sure that a whole range of needs are addressed and met, including transportation needs—often a main concern—and ensuring that prescriptions are filled and taken. "These interventions may seem simple, but they may impact whether or not a patient completes their treatment," she says.

#### Cost

Feliciano and colleagues are looking at how the costs of cancer care impact patients. The cost of drugs; lost wages from missed work; treatment for side effects, such as nausea and pain; and the cost of parking and transportation can add up to what feels like an insur-



Surviving and Thriving: Darlene Stewart, a patient of Feliciano's, is a retired teacher and a twotime cancer survivor. She battled breast cancer in her 20s. Now, she is combating advanced lung cancer, receiving a drug that targets a gene mutation in her cancer. The targeted therapy has kept her cancer in check for the last six years. "I love the Kimmel Cancer Center and Dr. Feliciano. It doesn't even feel like we're coming for a doctor's appointment. I feel great, and I have so much fun when I see her," says Stewart.

mountable burden. It is possible this "financial toxicity" from cancer care may impact patient choices and ultimately outcomes from their disease as well.

"There are so many costs that providers are unaware of and don't take into account," says Feliciano.
"Our goal is to understand these barriers to care so that we can do better for our patients."

With all these efforts, the Kimmel Cancer Center is dedicated to finding innovative ways to break down barriers so that all patients with lung cancer have access to the support and treatment they need to survive and thrive.

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Clinical Trials Life Lessons

## The Promise of **Immunotherapy**



Lung cancer expert Julie Brahmer led the landmark clinical trials that helped earn FDA approval for the immunotherapy drugs nivolumab and pembrolizumab in lung cancer.

Nivolumab (Opdivo) is now FDA approved for treatment of advanced non-small cell lung cancer in patients whose cancers progress on standard therapy, and pembrolizumab (Keytruda) became the first immunotherapy to gain FDA approval as the first-line treatment for non-small cell lung cancer patients whose cancer cells have a lot of a PD-L1 protein. Pembrolizumab works so well in this PD-L1 subset of lung cancer patients extending survival well beyond what chemotherapy was able to do-that these patients can now forgo chemotherapy and start with immunotherapy. A firstline combination of chemotherapy and pembrolizumab was also approved for patients with advanced lung cancer, making it the second FDA-approved immunotherapy combination.

Brahmer's clinical studies tested anti-PD-1 therapy in a variety of advanced cancers, including nonsmall cell lung cancer. She and the research team discovered that PD-L1 was expressed in human lung cancer cells and highly elevated when compared with normal cells. The remarkable activity of anti-PD-1 in a small number of lung cancer patients proved what Johns Hopkins Kimmel Cancer Center immunologists long believedif understood, the immune system could be used to fight any cancer.

prompted an aggressive immune attack against the cancers.

"These findings suggest that the timing of immunotherapy may be critical to successful cancer treatment in people whose lung cancers are operable." savs Forde.

He plans additional studies to see if they can extend this immune response to more patients by giving a longer course of anti-PD-1 or giving it in combination with other checkpoint inhibitors before surgery.

All these studies are aimed at PD-1 and a related partner protein on

#### CANCER DRUGS ARE HELPING TO BLOCK CHECKPOINTS AND SIGNALING THE IMMUNE SYSTEM TO ATTACK CANCER CELLS. AS A RESULT, THEY ARE HELPING TO SHORTEN THE AMOUNT OF TIME PATIENTS ARE TREATED.

Now, a new clinical trial led by Patrick Forde, in collaboration with surgeons Richard Battafarano, Stephen Broderick and Stephen Yang, may have uncovered evidence that—in some patients—immunotherapy should start even sooner. Forde's trial was the first to study anti-PD-1 immunotherapy before surgery. After just four weeks and two doses, all the patients had immune cells rushing to their tumors, and nine saw significant or complete reduction in the size of their tumors.



In this small study of 21 lung cancer patients with operable tumors, nine patients had a 90 percent or more reduction in tumor size. Forde and colleagues believe the immunotherapy tumor cells called PD-L1. PD-1 is what immunology experts call an immune checkpoint. Checkpoints are molecules on the surface of T cells and natural regulators of the immune response that cancer cells use to avoid immune recognition and attack. Drugs such as nivolumab and pembrolizumab block checkpoints and signal the immune system to attack cancer cells.

Laboratory research and early clinical trials point to PD-1 as one of the strongest influencers of an immune response to cancer identified so far.

Nivolumab has produced the longest follow-up to date of an immune checkpoint inhibitor. "Five-year overall survival quadrupled in non-small cell lung cancer, compared with what we would expect from chemotherapy," says Brahmer, director of the Thoracic Center of Excellence and the Bloomberg~Kimmel Institute for Cancer Immunotherapy lung cancer immunotherapy program.

"Based on these data, I think we can shorten the amount of time patients are treated. But we need to identify those patients who develop immune memory," says Brahmer. "I think we can safely say not all patients need indefinite treatment. We want to personalize therapy. We are continuing to look for biomarkers for response and long-term control."

#### **A WILD RIDE**

Patrick Personne was not surprised when his doctor told him he had lung cancer. The 62-year-old had been a smoker for more than 40 years, so when he began feeling ill and developed a nagging cough, lung cancer certainly came to mind. What did surprise him, however, was learning about a new type of treatment called immunotherapy.

"To me, lung cancer meant I was going to die. I thought I was done," recalls Personne. The avid motorcycle rider began planning his farewell ride, a trip to Patagonia, Argentina.

"When I was first diagnosed and saw the X-ray, there was this huge black spot on my lung. After just two treatments with the immunotherapy, it disappeared. It was like magic."

His doctor encouraged him to go to the Johns Hopkins Kimmel Cancer Center. "He told me, 'They are the best in the country," says Personne. He met with thoracic surgeon Stephen Yang and lung cancer expert Patrick Forde within days of his diagnosis and enrolled in a clinical trial using immunotherapy before surgery.

"When I was first diagnosed and saw the X-ray, there was this huge black spot on my lung. After just two treatments with the immunotherapy,



it disappeared. It was like magic," says Personne.

What he thought was going to be his last ride turned out to be a new beginning. His rides have become a metaphor for his triumph over lung

"I've traveled from the end of the world to the top of the world!" says Personne.

Before he left for his trip, he created a website where people follow his progress and donate to Forde's research. The ride raised more than \$10,000.

"I am grateful, and I wanted to

do something good. I think Dr. Forde is incredible," says Personne. "I've seen many, many doctors throughout my life, and there is no one like him." Personne feels certain that the immunotherapy Forde treated him with saved his life.

Personne also makes a personal gift in his two grandchildren's names each year on their birthdays. "I thought this would be much more beneficial than giving them another toy," he says.

Three years later, his cancer remains in check and, although he traded his motorcycle for a motor home, he still enjoys traveling the world.

#### Five healthy habits that can help support your wellness during and after treatment include:

- 1. STOP SMOKING
- 2. EAT WELL
- 3. BE ACTIVE
- 4. ENLIST SUPPORT
- **5. MANAGE YOUR CARE**

Whether it's you or a caregiver who's championing your cancer care, it's important to have someone who is advocating for your needs. This includes communicating with your cancer care team, coordinating appointments, and keeping track of symptoms and side effects.



#### [Cancer-fighting drugs]

# A'Pesty' Solution

#### How the Bugs We Live with Could Help Fight **Lung Cancer**

A NEW CLASS OF cancer-fighting drugs called checkpoint inhibitors is offering hope to patients with several kinds of solid tumors, particularly lung cancer and melanoma. The medications, which work by spurring the body's immune system to attack tumor cells, prolong life in roughly 20 percent of people who take them.

Why some patients do well but others fail to improve is a mystery, but emerging evidence suggests that at least some of the reason may lie with the trillion-odd bacteria that make up the body's microbiome.



Researchers at the Johns Hopkins Kimmel Cancer Center and Bloomberg~Kimmel Institute for Cancer Immunotherapy are studying



how the microbiome—the menagerie of germs that live in the gastrointestinal tract and other organ systems, including the lungs and skin-may interact with checkpoint inhibitors in ways that both make the drugs stronger and that potentially weaken their effectiveness. Their goals are to identify which strains of

bacteria sit on which side of the ledger and, if possible, to tweak a patient's microbiome in ways that make the cancer drugs even more potent.

Infectious disease and microbiome expert Cindy Sears is leading the research effort. "We're trying to attack on multiple fronts," says Sears.

CANCERS RESPOND TO Research in the area IMMUNOTHERAPY. has heated up recently, with several publications showing that groups of bacteria may alter the function of immune cells in ways that intersect with the function of checkpoint inhibitors. Some experiments found that a greater abundance in the gut of certain species of bacteria was associated with a stronger response to the drugs. Others showed the opposite—species of microbes that, when present, were linked to a poor response to the immunotherapy drugs.

At the moment, the research is in early days, Sears says, with many questions remaining unanswered. Which species of microbes are most important in the interaction, and how they alter the way the body processes

the cancer drugs, is unclear.

"One possibility is that there is priming, or education, of the immune system that either enhances or inhibits the capacity of the cells to respond to the tumor," Sears says. In other words, the presence of certain bacteria in the intestines conditions the immune system the way regular exercise strengthens muscles. When checkpoint inhibitors unlock the power of the immune system, it's better prepared to fight off cancer. Alternatively, exposure to certain strains of bacteria may sap the immune system, crippling T cells so that they're unable to rally that defense.

Another possibility is that proteins that the bacteria in the gut make are similar to those produced by cancer cells. "In this idea, the patient's immune system first develops an immune response to one or more bacterial proteins," Sears says. "When the tumor is treated with checkpoint

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blockade, the immune system is released to attack the tumor using the antibodies against bacterial proteins that 'mimic' tumor proteins."

Lung cancer expert Jarushka Naidoo is collaborating with Sears on the project. She is helping collect samples of bacteria from patients being treated with immunotherapy, tak-

ing swabs from stool, fluid from the lungs-which have their own microbiome—the mouth and urine. Using DNA profiling, they'll catalog all of the organisms present and try to build a profile of which ones are linked to a good response to the drugs and which appear to hinder their effectiveness.

Although the research is still in its early stages, Sears says she hopes the work will lead to the development of therapies-such as a "microbe cocktail" or even a vaccine—that will boost the immune response in cancer patients who receive immunotherapy. "We want these drugs to work for most patients, not just a small percentage of them," she says.

#### **Trending Research News**

# **CATALYST**

SU2C-LUNGevity Foundation-American Lung Association Lung Cancer Interception Dream Team: Julie



at developing new ways to intercept lung cancer—the leading cancer killer before it progresses to an advanced stage. The Dream Team brings together scientists and clinicians from many fields of lung cancer research, from prevention through early detection and treatment. The goal of the Dream Team's project, called InTIME, for Intercept Lung Cancer Through Immune Imaging and Molecular Evaluation, is to use state-of-the-art technologies to understand genetics, immunology, radiological imaging, and treatment response in patients with abnormal, precancerous lung tissue that puts them at high risk of developing lung cancer. Among the team's priorities are creation of a molecular atlas of precancers of the lung, development of two diagnostic tools that can be directly applied in the clinic for simple yet accurate detection of early lung cancer and new tests to identify which individuals are most likely to benefit from a number of treatment strategies, including emerging immunotherapies.



**Immunotherapy** Before Surgery: The anti-PD-1 immune checkpoint blocker nivolumab, given to

early-stage lung cancer patients before







Brahmer, M.D., and in-

terventional pulmonologist David Feller-Kopman, M.D., are among the investigators on the multi-institutional grant aimed

sion, an increase in anti-tumor T cells that remained after surgery and resulted in fewer relapses. The study, reported in the New England Journal of Medicine and led by Patrick Forde, M.B.B.Ch., in collaboration with surgeons Stephen Broderick, M.D., Richard Batafarano, M.D., Ph.D., and Stephen Yang, M.D., and experts in the Bloomberg~Kimmel Institute for Cancer Immunotherapy, also found that the number of gene mutations in the tumor correlated closely with response to treat ment and was a potential predictive marker for future studies. Stand Up to Cancer, LUNGevity, Bristol-Myers Squibb, Lung Cancer Foundation of America, the MacMillan Foundation, the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation, and the National Institutes of Health were among the funders. Broderick is currently serving on a steering committee for a multicenter global prospective randomized trial of immunotherapy before surgery combined with chemotherapy in early-stage non-small cell lung cancer. WEB EXCLUSIVE:

surgery, caused major tumor regres-

Listen to Dr. Forde explain the research bit.ly/2QuHmim



**Understanding How Radiation Heightens** Immune Response: A new study will decipher how stereotactic ablative radiotherapy

(SABR) heightens the immune response against cancer. SABR is a highly focused, intense dose of radiation treatment. It is very effective against lung cancer alone, and when paired with immune checkpoint inhibitors, which release brakes on cancer-fighting immune cells, it can

result in even better control of tumors in some patients. How checkpoint inhibitors work is well understood, but how radiation therapy impacts the immune system is not, says radiation oncologist Ranh Voong, M.D. A 10patient study, led by Voong and funded by the Lung Cancer Research Foundation, will examine biopsy samples obtained from patients before and after SABR treatment to better understand the effect radiation treatment has on immune cells, so that physicians will know how best to combine it with immunotherapy to achieve optimal responses in patients.

Immunotherapy Resistance: An indepth genetic analysis on tumor samples from patients before treatment with immunotherapy and again when the treatment stopped working led researchers Victor Velculescu, M.D., Ph.D., Valsamo Anagnostou, M.D., Ph.D., and Kellie Smith, Ph.D., to uncover a key way cancers become resistant to immunotherapy drugs known as checkpoint inhibitors. Their genetic analysis, published in Cancer Discovery, revealed that cancers get rid of genetic cues that flag the cell for destruction by the immune system. When the cancer cells shed these mutations, they discard the evidence that would normally lead them to be recognized by the body's protective immune cells. They are investigating how broadly the process occurs in lung and other cancer types to develop new ways to improve current cancer immunotherapies. Julie Brahmer, M.D., Patrick Forde, M.B.B.Ch., and Jarushka Naidoo, M.B.B.Ch., also collaborated on this research. LUNGevity and Stand Up To Cancer were among the funders.

Continued on page 14

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#### **Technology Guides Immunotherapy:** There are trillions of T cells within the



human body. Each one has the ability to see a different biochemical signature. Kellie Smith, Ph.D., is focusing on developing new T cell

receptor-based immunologic analysis and applying these technologies to lung cancer. Smith and Franck Housseau, Ph.D., both Swim Across America investigators, invented a sensitive test to detect anti-tumor T cells, recently reported on in Cancer Immunology Research. This technique, called MANAFEST, has the capacity to scour immense amounts of data to reveal the unique biochemical signatures in each patient's cancer that alert the specific immune cells T cells in that patient's cancer. The technology can be used to guide therapy, helping oncologists personalize immunotherapies by using drugs that will unleash an immune attack against individual cancers. Valsamo "Elsa" Anagnostou, M.D., Ph.D., Julie Brahmer, M.D., Patrick Forde, M.B.B.Ch., Kristen Marrone, M.D., and Jarushka Naidoo, M.B.B.Ch., collaborated on this research. Funders included the Bloomberg~Kimmel Institute for Cancer Immunotherapy, Bloomberg Philanthropies, and NIH Cancer Center Support Grant, the Lung Cancer Foundation of America/ International Association for the Study of Lung Cancer, Stand Up To Cancer, the Mark Foundation for Cancer Research, the Eastern Cooperative Oncology Group-American College of Radiology Imaging Network and the MacMillan Foundation.

#### **Test Monitors Treatment Response:**

A study, funded by Swim Across America, will explore an innovative combination of genomic and immune analyses to provide a basis for novel molecular approaches to identify patients most likely to respond to immunotherapy with checkpoint inhibitors. The project, led by Valsamo "Elsa" Anagnostou, M.D., Ph.D., will also help identify patients who will develop resistance to immune checkpoint blockade. The long-term

goal is the development of a predictive test to assess responses to cancer immunotherapy in real time. The test could lead to tailored cancer immunotherapy strategies and novel approaches to clinical trial design. Anagnostou is a LUNGevity Career Development Award and MacMillan Pathway to Independence Award recipient and a Swim Across America Scholar.

#### New Drug Combo: Jarushka Naidoo, M.B.B.Ch., will oversee a clinical trial



combining two epigenetic drugs with immunotherapy for patients with nonsmall-cell lung cancer. The clinical trial, co-led

by Stephen Baylin, M.D., is one of 10 Stand Up To Cancer (SU2C) Catalyst clinical trial projects. The inaugural SU2C Catalyst projects will explore new uses for an array of powerful medicines from three SU2C Catalyst charter supporters and six other pharmaceutical companies.

#### Addressing Treatment Resistance in



Small Cell Lung Cancer: Kimmel Cancer Center researchers received a \$3.1 million grant from the National Institutes of Health to



study the resistance of limited stage small cell lung cancer to a combination of chemotherapy and radiation therapy. Christine Hann, M.D., Ph.D., and Phuoc Tran, M.D., Ph.D., are

among the researchers who will lead the project expected to have a direct impact on the causes and possible treatment for chemoradiation resistance in

small cell lung cancer. Chemotherapy is the most common treatment for small cell lung cancer, but radiation therapy is frequently used in combination with chemotherapy when the tumor is confined to the lung and other areas inside the chest. Most patients respond to initial treatment, but the return of the disease due to chemoradiation resistance is almost universal. The researchers expect this research to provide a broader understanding of chemoradiation resistance in other cancers as well, pointing to new ways to target treatment resistance.

#### Lung Cancer at Sibley-Web Exclusive: Kimmel Cancer Center Director



William Nelson, M.D., Ph.D., talks with Ben Levy, M.D., clinical director of medical oncology at Sibley Memorial Hospital,

about new treatments for lung cancer patients and the growing cancer center at Sibley. bit.ly/2CTfTmQ

#### Julie Brahmer Receives Multiple Honors: Julie Brahmer, M.D., was elected to the International Association for the Study of Lung Cancer board of directors and was also featured on the cover of Chesapeake Physician magazine for her work in advancing lung cancer therapies. She also was honored by the Baltimore Orioles, with its Birdland Community Heroes Award, which recognizes those who inspire others through charity and community service. She was nominated by LUNGevity, which also honored Brahmer with its Face of Hope Award, for those who recognize the needs of and actively make a difference for people living with lung cancer.

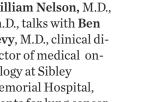




#### Managing Side Effects of Immunotherapy

#### A Conversation with Jarushka Naidoo

Immunotherapy is a promising new therapy that activates the immune system to attack cancer cells. It has a completely different side effect profile than chemotherapy, and that has caught some physicians off guard. Doctors—including emergency room physicians, dermatologists and gastroenterologists—need to learn about immunotherapy.



#### What types of side effects should doctors and patients look for?

if they believe them to be minor.

What do patients and doctors need to

The Johns Hopkins Kimmel Cancer

Center's Bloomberg~Kimmel Institute

for Cancer Immunotherapy is leading

munotherapy side effects. These side

symptoms, so their management re-

quires the cooperation of many ex-

perts. We have assembled a group of

specialists for every part of the body

that has the potential for adverse reac-

tions to immunotherapy, and they are

on call for us 24/7. It is important for

doctors and patients to call right away

if they experience any symptoms, even

effects can present with a wide range of

for recognizing and managing im-

the way and setting national standards

know about immunotherapy side effects?

Patients can experience side effects that include anything that ends in -itis. They are typically ones that involve inflammation, such as colitis (inflammation of the colon) and the worst of them, pneumonitis (inflammation of the lungs). These types of side effects aren't unexpected when taking medicines that tinker with the immune system, and inflammation is considered an immunerelated biochemical process. Aside from inflammation-related side effects, fatigue often tops the list of side effects. Some patients also experience low thyroid hormone levels. A new patient study is exploring a connection between immunotherapy and the development of inflammatory arthritis.

The toxic effects of immunotherapy drugs can occur anytime during a patient's treatment, even after patients stop taking the drugs. If side effects occur, they are typically at low-grade



#### WE HAVE ASSEMBLED A GROUP OF SPECIALISTS FOR EVERY PART OF THE BODY THAT HAS THE POTENTIAL FOR ADVERSE REACTIONS TO IMMUNOTHERAPY, AND THEY ARE ON CALL FOR US 24/7.

levels, but some have more severe effects. Treatment includes oral corticosteroids, and, for severe problems, hospitalizations may be necessary.

#### How are you educating patients about immunotherapy side effects?

Our patients come from all over the country. They could end up in emergency rooms or offices with doctors who do not understand patients' symptoms or mistake them for infections and provide incorrect treatment with devastating consequences. To prevent this, all of our immunotherapy patients are given a wallet card to carry with them at all times to share with any doctor they see. The card says, "I'm on immunotherapy. Please contact my oncologist." The card provides contact information and the name of the drug or drugs patients are

on. We also have a patient hotline, pager and email system.

#### What about doctors?

With support from the Cole Foundation, I am attending national cancer meetings with a Bloomberg~Kimmel Institute nurse to educate other doctors, and working with organizations like the National Comprehensive Cancer Network, of which I am a member, to share what we have learned and to establish standards for managing immunotherapy side effects. Julie Brahmer is cochair of the toxicity guidelines committees of the American Society of Clinical Oncology, National Comprehensive Cancer Network and the Society for the Immunotherapy of Cancer. We are also working on a web-based course for doctors.

#### Patient Creates Award to Distinguish the Best Lung Cancer Doctors and Nurses

Kimmel Cancer Center team is among inaugural recipients.



From left front, Christine Hann, M.D., Marilyn Holman, Hanika Reyes Rodavia, R.N. Back: Russell Hales, M.D., Matt Holman, Ph.D.

Despite being a scientist, Matt Holman was unsure of the best treatment plan and where to go to find it when his wife, Marilyn, was diagnosed with small cell lung cancer in 2016. He couldn't imagine what it must be like for the many patients and families who have no science or medical background.

"We had a lot of choices for where to go for treatment. I wanted to know what hospital had the best doctors and nurses and would provide the best care for my wife," says Holman, a scientist at the FDA.

He did his research, and ultimately, he and Marilyn selected the Johns Hopkins Kimmel Cancer Center, where she was treated by lung cancer experts **Christine Hann**, a medical oncologist, **Russell Hales**, a radiation oncologist, **Amy Vance**, a nurse practitioner, and **Hanika Reyes Rodavia**, a clinical research nurse.

"We were extremely impressed with the care Marilyn received," says Holman, so much so that they wanted to nominate the doctors and nurses for a patient care award.

Marilyn said people asked her why she chose Johns Hopkins for

her treatment. Her response was simple and direct: "Because they are the best."

Matt volunteered to take the lead on researching potential awards to find just the right one to acknowledge their Kimmel Cancer Center lung cancer team. The problem was, when he began to look, he could not find a single award that recognized stellar patient care.

His search turned up plenty of research awards, but nothing for patient care. Thinking he must have overlooked something, he reached out to his staff and colleagues at the FDA, but much to his surprise, no one knew of an award for outstanding patient care. In the absence of an existing award, Marilyn and Matt decided to establish a new award.

They had two goals—one was to recognize and honor the Kimmel Cancer Center team who cared for Marilyn, but primarily to help other lung cancer patients faced with the daunting challenge of choosing where to go for treatment. "We wanted to help others who were deciding where to take their loved ones," he says. The

Holmans wanted their award to serve as a guidepost for patients, helping direct them to compassionate and expert, multispecialty, team-based care.

They were impressed with the depth of knowledge of their Kimmel Cancer Center care team. "They get every expert involved in the care of lung cancer around the table to develop treatment plans for each patient," says Matt. "It's easy to take that kind of specialty care for granted, but trust me, it doesn't happen everywhere." Matt experienced this with his uncle, who he recently directed to the Kimmel Cancer Center, when he recognized his uncle was not getting the same level of care for his lung cancer.

The Holmans were equally impressed with their care team's willingness to discuss all of the options and share decision-making to come up with the best path forward.

"They were so compassionate, and although we knew Marilyn was one of many patients, it never felt that way. They treated her like an individual and were always willing to spend time answering questions and communicating complicated, scientific information in an easy-to-understand way," says Matt.

"My wife means more to me than anyone, and we were dealing with lung cancer. I had a long list of questions," says Matt. He recalls an appointment with Hales when he asked so many questions that Marilyn asked him to stop, worried they would annoy Hales. Far from annoyed, Hales looked at Marilyn and said, "It's all right. You are making decisions about your health, and I want you to be sure," recalls Matt.

Another time, a few days before Thanksgiving, Marilyn was in the outpatient clinic for a three-day series of chemotherapy treatments. The day before Thanksgiving, she experienced some complications. "The clinic was closing, but our nurse practitioner, Amy, stayed with us, consulting with the necessary experts to get us the answers we needed," says Matt. "She stayed late and waited for all of the experts to look at the test results so she could give us a plan to get us through the holiday weekend."

To make their patient care award idea a reality, the Holmans decided to reach out to the International Association for the Study of Lung Cancer (IASLC), which supports research

# THE HOLMANS WANTED THEIR AWARD TO SERVE AS A GUIDEPOST FOR PATIENTS, HELPING DIRECT THEM TO COMPASSIONATE AND EXPERT, MULTISPECIALTY, TEAMBASED CARE.

through young investigator awards. IASLC Foundation representatives agreed that a caregiver award was needed, and working with Marilyn and Matt, they established the IASLC Foundation Cancer Team Award. Marilyn, an artist and elementary school teacher, designed the award. Hann, Hales, Vance and Rodavia were among the inaugural recipients.

"The truth is, if Drs. Hann and Hales, and all of the other doctors and nurses had not provided such exceptional patient care, this award would not exist," says Matt.

Marilyn recently passed away, but because of her and Matt's persistence, patients, survivors and caregivers have a way to honor and recognize multispecialty lung cancer teams—experts in all areas of lung cancer treatment—that provide exceptional care. The international award helps the best of the best stand out among the many lung cancer providers and can help ease the burden for newly diagnosed patients around the world who are searching for the best lung cancer care.

# THRIVING AND SURVIVING LUNG CANCER

Patients, families and friends are invited to join us in November to celebrate Lung Cancer Awareness Month and participate in an interactive discussion on the latest research and treatments, share stories of survivorship, and meet our lung cancer health care team.

Visit **hopkinscancer.org** or call 410-550-1711 for event details.

For more information on this and other events, please call 410-550-1711.





#### Help Us Make a Difference

Each contribution to the Johns Hopkins Kimmel Cancer Center makes a difference in the lives of cancer patients here at Johns Hopkins and around the world.

Our physician-scientists are leading the way on many of the scientific breakthroughs in lung cancer, and your donation will support patient care and innovative research that is translated to better, more effective treatments. We are also focusing on ways to prevent cancer and support survivors.

You may designate a gift to a specific faculty member.

To make your donation online: **hopkinscancer.org** and click "Make a Gift"

To mail your donation: Johns Hopkins Kimmel Cancer Center 750 E. Pratt St., Suite 1700 Baltimore, MD 21202 Please note that you would like your gift to support the thoracic cancer program.

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