

Yale Cancer Center

# centerpoint

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MAGAZINE



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to Target the Rise in Liver Cancer



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Dr. Jeff Geschwind

Peter Baker **photographer**

yale cancer center

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**New technologies, spurring scientists' ability to innovate**, are driving cancer research and propelling breakthroughs in basic, translational, and population cancer research. At Yale Cancer Center and Smilow Cancer Hospital at Yale New Haven, we are continuously investing in technology to push pioneering research and clinical care forward. In this issue of *Centerpoint*, you will read about Dr. Jeff Geschwind, Professor and Chair of Radiology and Biomedical Imaging. Dr. Geschwind is leading research to improve imaging and therapeutics to target and treat liver cancer – a cancer whose incidence and mortality are steadily rising.

Just as we invest in technologies and research, the leadership of Smilow Cancer Hospital and Yale New Haven Health System (YNHHS) is continually advancing our clinical operations. This spring, YNHHS opened a new facility in Trumbull that includes our Cancer Care Center. The Park Avenue Medical Center unites oncology cancer care with radiation oncology, diagnostic imaging, outpatient surgical suites, and the Norma Pfriem Breast Center. We are pleased to have a modern location to offer our patients cancer care in Fairfield County and grateful for our collaborations with Bridgeport Hospital in the new Park Avenue Medical Center.

The summer months will be busy here as we look forward to opening the new Phase I Clinic adjacent to Smilow Cancer Hospital. This new facility is dedicated to the care of patients on phase I clinical trials and will feature 12 infusion chairs and 4 exam rooms dedicated to phase I clinical research and care. I look forward to sharing more information on our Phase I Clinic with you in the fall issue of *Centerpoint*.

Our faculty continues to receive top national honors for their dedicated work. Recently, Mark Lemmon, PhD, Co-Director of our Cancer Biology Institute, was named a Fellow of the Royal Society, the United Kingdom's national academy of science; Patricia LoRusso, DO was elected to the Association of American Physicians, one of our nation's oldest medical honor societies; Lajos Pusztai, MD was named a Susan G. Komen Scholar; Harriet Kluger, MD was inducted into the American Society for Clinical Investigation; and Joseph Schlessinger, PhD was appointed a Fellow of the American Association for Cancer Research.

I am pleased that we continue to see momentum at Yale Cancer Center and Smilow Cancer Hospital with investments in technology, basic, translational, and prevention research, and our faculty. This issue of *Centerpoint* shares some of our innovations with you, and we look forward to more as 2016 progresses. Enjoy your summer.

Sincerely,

Peter G. Schulam, MD, PhD  
Director, Yale Cancer Center and  
Physician-in-Chief, Smilow Cancer Hospital (Interim)



# NEW TECHNOLOGIES TO TARGET THE RISE IN LIVER CANCER

Steve Kemper writer Peter Baker photographer

In March, the National Institutes of Health's *Annual Report to the Nation on the Status of Cancer, 1975-2012* carried the welcome news that cancer rates are falling for most forms of the disease. But the report also included a special section highlighting one exception: "Liver cancer deaths are on the rise in the United States, increasing at the highest rate of all the common cancers during the period 2003-2012."

"We are just at the beginning of the uptick in liver cancer," said Jean-Francois (Jeff) Geschwind, MD, Professor and Chair of Radiology and Biomedical Imaging, who has spent two decades researching liver cancer and developing new ways to fight it. "Ten years ago there were 12,000 new cases a year in the United States. Now it's 28,000."

Worldwide, the statistics are even more alarming. Only lung cancer kills more people every year than liver cancer. Most of these fatal cases occur in less developed parts of the world. "In Asia and Sub-Saharan Africa, it is a massive problem," said Dr. Geschwind. "I would not be surprised if, within five years, liver cancer overtook lung cancer."

About 80-90% of primary liver cancers develop from cirrhosis, a chronic inflammation of the liver. The three main causes of cirrhosis—and therefore the main precursors of liver cancer—are hepatitis B, hepatitis C, and now obesity induced non-alcoholic steatohepatitis (NASH). The World Health Organization estimates that 240 million people have chronic hepatitis B, and 130 to 150 million people have chronic hepatitis C.

"Do the math and you can see how many are going to develop liver cancer," said Dr. Geschwind. Several new drugs

have shown tremendous success against hepatitis C, but are beyond the financial reach of many infected patients.

Liver cancer is mostly asymptomatic in its early phases and often goes undetected until more advanced stages, when surgery is not possible, which explains why survival rates are so poor. And because the patient's liver is usually severely damaged by cirrhosis as well as cancer, traditional chemotherapy may kill the liver, along with the tumor. "That's why it's so critical to treat the cancer only where it actually occurs in the liver," said Dr. Geschwind, "and to protect as much of the healthy liver tissue as possible."

That's the idea behind a therapy called transarterial chemoembolization (TACE). Dr. Geschwind's research has contributed significantly to it. In TACE, catheters the size of a human hair are loaded with a vehicle consisting of an oily medium or microbeads filled with chemotherapy drugs, usually doxorubicin. Then, with help from sophisticated imaging technology, the catheters are maneuvered via the arterial supply directly into the liver tumor where the vehicle is released, saturating the tumor with chemotherapy over several weeks. Next, other beads are deposited via the same catheter to reduce the arterial inflow to the liver tumor to block the blood flow to the tumor. In essence, TACE simultaneously poisons the tumor while eliminating its blood flow.

"In every other organ," said Dr. Geschwind, "blood flows in through the artery and out through the vein. But in the liver, 80% of the flow comes from the vein, which brings the blood back from the gut to the liver so the liver can do its job as the body's chemical factory. Liver tumors, on the other hand, draw

their blood supply almost completely from the artery. So we can exploit this unique property by threading catheters and navigating through the arterial anatomy, thereby targeting the tumor while preserving the healthy liver tissue.”

TACE was pioneered in Japan in the 1980s but didn't become commonplace in the United States until nearly two decades later. Since then, TACE has steadily improved through advances in drugs, drug delivery, and imaging. Dr. Geschwind has been at the forefront of the research to improve TACE and is one of TACE's main innovators. He is in the fifth year of a five-year NIH grant that funded research to improve TACE through better imaging, namely 'seeing, targeting, treating, and assessing tumor response after therapy.' "By making sure every tumor is visualized, we can ensure that we will never miss the target," Dr. Geschwind explained.

A specific example of imaging technology that was developed by Dr. Geschwind's team in collaboration with Philips Healthcare is the ability to visualize the entire liver. This is an especially important problem in the United States where many patients are overweight and therefore performing a cone beam CT scan during a TACE procedure can be challenging. "What we managed to accomplish is to develop software that adjusted the centering process thereby establishing the image rotation around the liver rather than on the patient. This software is now a new commercial product called Open Trajectory."

To improve the visualization of the liver tumors, Dr. Geschwind's team developed dual-phase cone beam CT (DP-CBCT). Unlike earlier methods, it performs two scans from one injection of dye. The first scan reveals the arteries feeding the tumor; these become the pathways used to deliver chemotherapy, which are then blocked off to starve the tumor. The second scan, which is slightly delayed, identifies and visualizes the tumors. After the procedure, another

DP-CBCT scan shows how much damage the treatment has done to the tumor. Instead of waiting to learn whether a treatment has worked, both the patient and the care team receive immediate feedback.

To better utilize DP-CBCT, Dr. Geschwind and Philips Healthcare devised software that provides live 3D images to help clinicians navigate through arterial pathways and deliver TACE. "It highlights the roadway to the tumor and calculates the way to get there," said Dr. Geschwind, "like Google Maps."

A peculiarity of liver cancer is that even when the tumors respond to treatment, they often don't shrink. "So we needed a new way of assessing response," explained Dr. Geschwind. He and his team created yet another software that

**"It highlights the roadway to the tumor and calculates the way to get there," said Dr. Geschwind, "like Google Maps."**

precisely measures tumor volume and necrosis. Called qEASL, it replaces the usual one- or two-dimensional images with a segmented 3D map of the tumor. Injected dye reveals which parts of the tumor are alive or dead. "So instead of an estimate of the necrosis," explained Dr. Geschwind, "we have a real number that provides an accurate quantification of tumor kill (70, 80%, etc.) and, as a result, we now have a much better sense of the success of our therapy. We can also determine with greater certainty when re-treatment is not necessary because we know the tumor is dead."

TACE is now recommended only for patients with intermediate stage liver cancer, but Dr. Geschwind is working on ways to expand its applicability. He wants to use it against more advanced

cancers where TACE could be combined with other therapies, such as agents that block the formation of new blood vessels or with immuno-oncology to exploit the profound inflammatory reaction that TACE causes. Here, checkpoint inhibitors could be given simultaneously with TACE or immediately after TACE to unleash the immune reaction. At the other end of the spectrum, patients in need of a liver transplant may be required to wait for a long period of time given the scarce availability of organs. In such cases, TACE is an extremely useful and effective therapy to prevent disease progression, keeping patients eligible to receive a transplant. He recently received another five-year grant from the NIH to pursue his work on TACE and he has several clinical trials planned or underway at Smilow Cancer Hospital.

He's incredibly excited about doing this work at Yale, which recruited him last year from Johns Hopkins. Yale enticed him with the position of department chair and a brand new state-of-the-art lab, not to mention access to world-class facilities at the Positron Emission Tomography (PET) Research Center and the Magnetic Resonance (MR) Research Center. But what sealed the deal was something Dr. Geschwind recognized during the interview process.

"There is something truly special at Yale. The level of enthusiasm and desire to achieve greatness is incredible," he said. "The people I met during the interview process were amazingly supportive, friendly, and warm. This was true of the other department chairs, the hospital, and medical school leadership. Everyone seemed to be on the same page and functioned in unison like a top class orchestra. I instantly felt like I belonged. I know that we have all the elements to create a Liver Cancer Center of Excellence at Yale. We have top class medical oncology, surgery, transplant, and hepatology. I am absolutely convinced that with the proper support, our center will become the envy of the world." 🔄

# Looking Beyond LUNG CANCER

Emily Fenton writer Peter Baker photographer



**B**ob Carlson cannot describe what a symptom of cancer feels like, even though he was diagnosed with stage IV lung cancer five years ago. A growth was found by chance during a CT scan and later a thoracic surgeon made the diagnosis of stage IV non-small cell lung cancer, which had metastasized to his adrenal gland. It was found early enough that he did not notice any symptoms, but not early enough for standard treatment to have much effect. After several rounds of chemotherapy, Bob was told a clinical trial might be an option and that he should meet with Dr. Roy Herbst at Smilow Cancer Hospital, a nationally recognized leader in lung cancer treatment and research.

The trial that Bob was hoping to participate in was Dr. Herbst's BATTLE program, which uses molecular analysis of tissue biopsies to help determine the best treatment. However, Bob's blood pressure was too high and they could not get it lowered in time for the trial. Luckily, Dr. Herbst was also leading another trial, an early-phase immunotherapy trial looking at a new anti-PD-L1 antibody called atezolizumab (previously known as MPDL3280A). The trial was originally supposed to last

one year, but Bob has now been on the trial for 3 years. In the first year, the tumors in Bob's lungs and adrenal gland shrunk significantly, and the drug continues to keep his cancer at bay, slowing its growth.

Atezolizumab is an immunotherapy drug that works by helping the immune system find and attack cancer cells. It begins with sequencing the genes of the individual's tumor to identify the protein PD-L1, which blocks the immune system from attacking the cancer. "This trial is for patients whose tumors have high expression of PD-L1 and whose disease worsened during or after standard treatments," said Dr. Herbst. "Since Mr. Carlson started on the trial, atezolizumab has completed phase III trials and is being fast-tracked for approval from the FDA. Patients like Bob have made this possible."

As explained in a recent paper published by Dr. Herbst and his colleagues in *Nature* (27 Nov 2014), the response to this drug has been significant in a large cohort of patients, with few side effects. This trial was unique in the fact that it was a first-in-human study, meaning they were hoping to establish whether the drug behaved in human subjects as



**"When my wife and I first learned that I had cancer, she was terrified of losing me. Now each night before bed, I tell her, I am not going to die today, and thanks to trials like the one I am on, I am hopeful that I have many more nights like that ahead. We will see what tomorrow brings, but today I am alive and that in itself should be enough for anyone, cancer or not."**

predicted from preclinical studies and was safe to undergo further development.

About a year ago the growth on Bob's adrenal gland returned, so he had surgery to remove the gland and a few months later a new growth was found at the bottom of Bob's lung, but thankfully it is slow growing. Other than resulting from the surgery, Bob commented that he has had no side effects from the immunotherapy. When Bob learned that he had cancer, he decided to retire and he commented that the



diagnosis, along with the financial impact of not working, was a lot to handle. After going through chemotherapy and experiencing side effects such as mouth and nose bleeds, fevers and low white blood cell counts, in addition to nausea, his hope is that drugs like this can be fast-tracked for approval more often so that patients can receive it as a first-line therapy, which will enable them to continue to work and have a high quality of life.

"The last 2 ½ years are years that I didn't think I would have," said Bob. "Once my wife and I got over the initial shock of the diagnosis, acceptance was key for me. I know the cancer may win eventually, but who knows when eventually will be. People ask me all the time, 'how long do you have?' and I ask them the same thing. No one knows for sure, I just have the knowledge that each day is a gift and should be lived to the fullest. I don't dwell on the fact that I have cancer, I am lucky that I don't feel sick and I still have a life to live."

Entering into a clinical trial was a no-brainer for Bob. The chemotherapy regimen was making him so sick that he couldn't live a normal life, and his other options included removal of the lung, radiation therapy, or to do nothing. None of those options worked for Bob, who is a former long distance runner and an avid bird photographer. "A clinical trial gave me a chance to be alive," said Bob. "If it didn't work, I knew it would be helping future generations, so it was a win-win in my mind."

Marianne Davies, DNP, ACNP, AOCNP, has taken care of several patients as part of this trial, including Bob, and commented, "Bob's prior treatment was impacting his daily life and was

debilitating for him. On this trial he has experienced minimal to no side effects and his response has been great. It's very rewarding to see him doing well and able to do the things that he loves."


Bob described the team at Smilow as a network that worked together to treat him and his cancer. He never felt rushed during his appointments or that there were questions he couldn't ask of the nurses or doctors. "Everyone that you interact with knows you and knows your case. It made me feel very confident in the decisions that were being made."

Every 12 weeks Bob is scheduled for a CT scan to monitor any growth, and he receives his treatment once every three weeks. Even though Bob knows this is not a cure, he realizes that there is always something new in the pipeline, and that advancements are constantly being made. For lung cancer patients especially, Bob commented, this should provide a source of great hope. Bob's other advice is to seek out a major cancer hospital that has the expertise for your type of cancer. "Not all oncologists are created equal or have access to these cutting-edge trials," said Bob. "It's important to find someone that you can relate to as well, because



hopefully you will be with them for a long time. Dr. Herbst explained everything to me and gave me honest answers. He knows how the drugs work and how to care for patients."

For Dr. Herbst, seeing a patient with advanced lung cancer doing so well is inspirational. He has come to know Bob and his wife very well over the years, something he could have only dreamed of when he first started seeing patients. "That just didn't happen," said Dr. Herbst, "but thankfully that is changing. It is so satisfying to see translational research from Yale Cancer Center bringing new drugs from our labs to Smilow Cancer Hospital to help patients like Bob. With funding from our new Lung SPORE our goal is to figure out ways to help even more people." 🔄



Diane Krause, MD, PhD

# MANUFACTURING CELLS THAT FIGHT CANCER

Steve Kemper writer Peter Baker photographer

The new Advanced Cell Therapy (ACT) Laboratory widens Yale Cancer Center's horizon of possibilities for developing cutting-edge therapies. "It's a state-of-the-art facility," said Diane Krause, MD, PhD, Medical Director of the lab; Professor of Laboratory Medicine, Cell Biology, and Pathology; Associate Director of Yale Stem Cell Center; and Medical Director of the Clinical Cell Processing Laboratory. "Only the top cancer centers have a laboratory like this. Yale needs this lab to do clinical trials using cells."

The facility is a Class 10,000, Good Manufacturing Practices (GMP) laboratory with three ISO 7 rooms. Those specs are required to manufacture cells that can be transferred into patients. In lay terms, the specs signify a super-clean sterile environment. The air is HEPA-filtered, which means that 99.97 percent of all airborne particles are removed. Everyone in the lab wears hats, gloves, booties, and coveralls made of particle-free materials. "A lot of effort goes into maintaining that clean-room atmosphere," said Dr. Krause, "and we test it daily to prove that it's clean."

The lab allows Yale's scientists to create cellular therapies that go far beyond the type familiar to most people—bone marrow transplantation. In that treatment, a cancer patient gets high doses of chemotherapy to destroy the blood-making stem cells in their bone marrow. These cells are replaced by cancer-free bone marrow, either from the patient or from a donor, which is infused back into the patient.

New cellular therapies take a huge leap beyond that. One of the most exciting innovations is to inject a patient with manufactured cells that recognize cancer and supercharge the immune system's response against it. These cells may be from the patient or from someone else. "It's huge," said Dr. Krause, "and it's where the field is now."

While the physical space for the Advanced Cell Therapy Laboratory is new, the team under Dr. Krause has been working at the cutting edge of Cell Therapy and Regenerative Medicine for many years at Yale. At the moment, Dr. Krause's laboratory team is assisting two immunotherapy clinical trials at Yale for metastatic melanoma. Both trials are



for pharmaceutical companies. The lab helps to harvest the cells, but then sends them to the drug companies' labs for further processing and manufacture before the cells return to Yale for infusion back into the patients. The principal investigator on both trials is Harriet Kluger, MD, Professor of Medicine (Medical Oncology).

"Cell therapy for melanoma has been used for years by the NCI," said Dr. Kluger. "We are now one of a handful of institutions that offer this type of therapy, and the reason there are so few is that cell therapy is quite intense. These pharmaceutical trials are a means to get our feet wet, but our goal in the near future is to conduct our own trials, where we do all of the cell processing here, enabling us to manipulate cells in novel ways based on experiments done in labs at Yale. That's where Diane's facility is key."

The next Yale-initiated clinical study is expected to begin this fall, once it gets the necessary approvals from the FDA and Yale. The trial will test a cellular immunotherapy that uses greatly expanded numbers of tumor-infiltrating lymphocytes (TILs), which are white blood cells found in tumors, to target the cancer.

TILs therapy builds on discoveries about the mechanisms of the immune system. "We know that cells within the immune system attack cancer," said Michael E. Hurwitz, PhD, MD, Assistant Professor of Medicine (Medical Oncology), who will be the principal investigator on the clinical study, "and we know that some cells actually invade into the cancer. That's what TILs are—immune cells that have invaded into the cancer itself. It turns

out that these cells are the most active against the cancer, which makes sense because they're found at their target sites inside the tumor." The problem occurs when cancer cells overpower these TILs and begin spreading.

The Yale trial will test TIL therapy against metastatic melanoma. First, under absolutely sterile

**"The patients achieve long-term cures. The process is widely known but not widely performed, because the work is so involved. Only four or five other centers can do it."**

conditions, Dr. Hurwitz's team will remove the main tumor, which isn't usually done with metastatic cancer. From there, the highly trained team in the ACT Laboratory will take over. The tumor will be dissected into small bits, and enzymes will be added to break down those bits into what Dr. Krause calls "a single-cell slurry." The lymphocytes—the immune cells—will be separated from the cancer cells and then put into an incubator, where they will be expanded with help from growth factors.

"We nurse them for about two weeks," explained Dr. Krause, "and then we rapidly expand them for another two weeks, to get a 6,000-fold expansion. So we're manufacturing the patient's own immune cells from the patient's own tumor. Then the clinicians infuse those cells back into the patient immediately following a high dose of chemotherapy to suppress their immune system. The 6,000-fold expansion of the lymphocytes overwhelms any inhibitory effects of the immune system and destroys the cancer. And the patients achieve long-term cures. The process is widely known but not widely performed, because the work is so involved. Only four or five other centers can do it."

"This is very complex and requires a lot of coordination," said Mario Sznol, MD, Professor of Medicine (Medical Oncology); Program Leader of the Melanoma Program; and Co-Director of the Yale SPORE in Skin Cancer, which is providing some of the clinical trial's funding. "It's impossible to do without people like Diane and without a facility that can generate these cells, and also without having someone like Mike [Hurwitz] interested in being the lead. The lab's success also depends on Alexey Bersenev, MD, PhD, Technical Director of the ACT Lab and Associate Research Scientist, who's a world expert in the production of these cells and the expertise of cellular immunologist Marina Komarovskaya. None of it is possible without all of this collaboration."

Dr. Hurwitz expects to enroll 10 patients in the trial. In addition to demonstrating Yale's ability to



Marina Komarovskaya pulls cell samples from Nitrogen tanks.

provide TIL therapy, he and Dr. Krause will be looking for ways to improve it, perhaps by enhancing the generation of cells or, once the cells are infused, the conditions inside the patients, perhaps by using drugs to boost the TILs aggressiveness and distribution.

The trial also will open up other avenues of research. For instance, Dr. Hurwitz expects to analyze the removed tumors to see if some are more susceptible to treatment than others. Dr. Kluger also sees many possibilities. "Once the whole operation is running," she said, "it opens the door for experimental interventions. For example, we can do genetic engineering of the immune cells before we reinfuse them. We can expand the cells in the petri dish and expose them to cancer cells. We can make new cancer-specific immune cells. The Advanced Cell Therapy Lab provides us a lot of

opportunity to be at the cutting edge of immunotherapy for solid tumors and liquid tumors."

Drs. Hurwitz and Kluger both hope to run clinical trials in the near future that use TILs against kidney cancer. Dr. Hurwitz also mentioned bladder cancer and lung cancer, and added, "And I think the list will grow."

Dr. Krause is eager to jump into the manufacture of other innovative cell therapies that use dendritic cells, natural killer cells, and lymphocytes expressing chimeric antigen receptors (CARs). Her new lab can handle all of those processes. "We're just waiting for the opportunity," she said.

Drs. Hurwitz, Kluger, and Sznol all are certain that such opportunities are around the corner, thanks to the new facility. "Once you have it in place, it's like *Field of Dreams*," said Dr. Sznol. "If you build it, they will come." ☺



PETER BAKER

## Caring For Our Veterans

**T**he Veterans Affairs (VA) Comprehensive Cancer Center in West Haven, an affiliate of Yale Cancer Center, serves veterans throughout Connecticut and southern New England. Each year it cares for about 600 new cases of vets diagnosed with cancer.

“We have almost all the specialties of surgery,” said Michal G. Rose, MD, Director of the VA Cancer Center, “and we offer almost all types of chemotherapy and biological therapy.” The West Haven VA was also among the first in the country to do robotic surgeries for various cancers in the lung, prostate, head, and neck. The hospital provides a full array of support services, including social workers, care coordinators, and a hospice team. “The one thing we do not offer is radiation therapy,” said Dr. Rose, “so most of our patients go to Smilow Cancer Hospital for that.”

Dr. Rose and her fellow VA oncologists sometimes consult colleagues at YCC about rare cancers and other complex issues. “We’re a small hospital,” she said,

“but we have large hospital capabilities because of Yale’s expertise and resources.” Yale, too, benefits from the affiliation. Oncologists at the VA hold Yale academic appointments, and the hospital is an important training ground for the fellowship program.

Because the smoking rate among veterans is higher than in the general population, VA doctors see a lot of lung and bladder cancers. Other cancers—prostate, lymphoma, and sarcoma, as well as lung cancer—are associated with exposure to Agent Orange, a defoliant used in Vietnam. Some veterans respond to the stress of military experience by abusing alcohol and other drugs, which also increase their risk of cancer.

Early diagnosis is critical, and Dr. Rose is especially pleased with the VA’s screening program for lung cancer, which has assessed more than 3,000 patients. “We’ve been able to do that because we have such a good care coordination program,” she said. “We were the first VA to offer it. You won’t find it anywhere else, really, to the extent that we’re doing it.”

She began the program soon after becoming director in 2005. She noticed that some patients were falling through the cracks because the complications of cancer care—the many appointments and tests, the many disciplines involved—could overwhelm patients who had psychosocial problems or little family support. Dr. Rose combined the VA’s excellent electronic medical records system with a new software program that analyzes each day’s list of scans and flags any that suggest cancer. Each morning, a care coordinator makes sure that every flagged patient gets

scheduled for any required services. The coordinator also becomes the veteran’s contact person throughout the cycle of care, lessening anxiety and delays. “Patients get diagnosed and staged quicker,” said Dr. Rose.

One area where cancer care for veterans has lagged is enrollment in clinical trials. Recent data showed that veterans are less likely than other populations to have this opportunity.

“It’s a well-kept secret that the only social healthcare system in the country actually gets good results.”

They often are excluded because of co-morbidities that drug companies fear could weaken results.

“But there’s plenty of literature showing that because of so many exclusions, the results are less applicable than they should be,” said Dr. Rose. “We should be studying drugs for the people who actually need them.”

There’s a push to correct this. One example is a nationwide clinical trial called Lung-MAP. The West Haven VA was the first VA to enroll patients on this study, which is testing five cutting-edge immunotherapies and targeted therapies against lung cancer. Dr. Rose expects VAs to attract more such trials as drug companies realize that the VA’s system of linked electronic medical records is a massive national database of potential enrollees for almost any form or mutation of cancer.

Politicians, pundits, and headlines

often create the impression that the VA system is an embarrassing mess. Studies tell a different story. VA hospitals routinely outperform non-VA hospitals in fundamental categories—quality of care, patient satisfaction, and cost. Many attacks on the VA can be traced to entities that would profit if the system were privatized.

“It’s political,” said Dr. Rose. “The VA does have problems, and

some VAs are better than others. But whenever a study looks at quality indicators, the VA does better than the American healthcare system, because it’s integrated and the incentives are right. It’s a well-kept secret that the only social healthcare system in the country actually gets good results.”

That’s certainly the view of Dr. Rose’s patient Dudley Day, a Vietnam vet from Wallingford who has been going to the West Haven VA since 2007. During a regular check-up he was diagnosed with small cell lung cancer. He received chemotherapy at the West Haven VA with some benefit, but then experienced progression of his cancer. This April, with Dr. Rose’s help, he enrolled on a clinical trial at Smilow Cancer Hospital using an immunotherapy drug.

“The care is exceptionally better than private,” he said. “They are hands-on, wonderful, and I love them.”



## Measuring Emotional Distress

A diagnosis of cancer can trigger waves of distress. At Smilow Cancer Hospital, social workers, financial counselors, and chaplains, among other resources, have long been available to patients. Yet these referrals tended to be catch-as-catch-can, because there wasn't a system to detect patients in distress or to discern the causes.

Two developments changed that. First, the American College of Surgeons began requiring cancer programs to assess a patient's psychosocial distress levels several times during the continuum of care. Second, Smilow leadership noticed that on patient surveys the rating for services dealing with distress lagged behind those in other categories.

"When you don't screen cancer patients at pivotal points in their cancer journey, you miss things," said Bonnie Indeck, MSW, LCSW, Manager of Oncology Social Work at Smilow Cancer Hospital, "and we didn't want to miss things. We wanted

to make sure that our patients were receiving the holistic care they need."

Smilow staff designed a pilot program to attempt just that. They adopted a screening tool developed by the National Comprehensive Cancer Network (NCCN) called a Distress Thermometer. It's a paper questionnaire that asks patients to rate their level of distress during the past week on a scale of zero to ten. Alongside the thermometer, potential reasons for distress are listed under various domains, and the patient checks off any that apply. The domains cover practical issues such as childcare and finances, emotional issues such as depression or family problems, physical issues such as side effects of treatment, and spiritual concerns. A patient who self-rates a distress

level of four or higher is immediately referred to an appropriate resource, usually a social worker.

The pilot launched in October 2013 in two Smilow Care Center locations. It ran for six months and surveyed 864 patients. The goals were to measure patients' levels of distress, to pinpoint the main causes, and to see if interventions brought relief and greater patient satisfaction. The results were clear.

"Patients were very appreciative that we acknowledged that this was something that needed to be addressed," said Catherine Lyons, RN,

MS, Executive Director of Patient Services at Smilow Cancer Hospital, "and glad that their care team was concerned about these issues and not just about their cancer."

Most patients also reported that the staff's interventions made a difference in their ability to cope with diagnosis and treatment. "When you're diagnosed with cancer—and I can

The pilot also affirmed that the distress screen should be given several times during a patient's care. Pivotal points may occur during the depths of treatment, or when an initial treatment fails, or when the cancer recurs. Another surprising stress point pops up when treatment ends, an emotional time because the patient must say goodbye to staff and



**There's nothing more important than feeling that your doctor and your team not only care about curing your cancer, but about you as a person.**




speak from personal experience," said Ms. Lyons, "—there is a tremendous amount of anxiety. But once you spend time with your doctor and care team, and you have a plan of attack, a calmness comes over you, because now you know what you have to do."

Diane Corjulo, RN, BSN, Clinical Program Manager for five Smilow Cancer Hospital Care Centers, including the two pilot locations, often saw that happen with new patients. "They might circle a ten on their first visit," she said, "but after they talked to a doctor, they were a three, because they just needed information and the understanding that we were going to do our best to give them whatever they needed." That sometimes meant referrals to long-term counseling or support groups.

fellow patients, and transition to a life without cancer.

When the pilot began, the staff worried that the program would add more work to busy schedules. Instead the extra work was minimal, and nurses and doctors found themselves enthusiastic because the screening and interventions so obviously helped patients and led to better care.

The program has since expanded to Smilow's main hospital and to all of the Care Centers. "There's nothing more important than feeling that your doctor and your team not only care about curing your cancer, but about you as a person," said Ms. Lyons. "I think that by asking these questions, we're imparting that we care for you, and that we're going to bring everything we have to help you during this journey." 

Victoria Bernardo, RN reviews the distress screening with Ms. Remette at Smilow Cancer Hospital before her appointment begins.



Drs. Kert Sabbath, Anamika Katoch, and Victor Chang



PETER BAKER

## Smilow Cancer Hospital Care Center - Waterbury

The Waterbury Care Center was selected as the first application submitted from Smilow for QOPI certification, the first office for EPIC integration, and also a pilot site for Smilow’s oral chemotherapy initiative.

### PRACTICE AT A GLANCE

- 1,400 patient visits per month
- 600 chemotherapy treatments per month
- 29 staff members
- 27 clinical trial accruals per year
- Radiation oncology, diagnostic radiology, social work, nutrition, and support groups all offered on site.

*“I’m proud of the physicians and staff at our Waterbury Care Center for their dedication to our patients each day. We work together as a team to make sure everyone’s needs are met and collaborate with the resources at Smilow Cancer Hospital to give our patients access to the best treatment options available.*

— Dr. Kert Sabbath, Medical Director

**SMILOW CANCER HOSPITAL CARE CENTER AT WATERBURY**  
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Phone: 203-755-6311



PETER BAKER

Q+A

## meet the physician

# Jaykumar R. Thumar, MD

Adjunct Assistant Professor of Medicine

### You recently transitioned into community practice at Smilow Cancer Hospital at Yale New Haven’s Saint Francis Campus. How do you bring Smilow’s mission of translational research to your patients in Hartford and Enfield?

There are various ways through which we are bringing the research to the community in Hartford and Enfield. We present patient cases and participate in multidisciplinary tumor board conferences at Smilow Cancer Hospital. This allows us to collaborate with our colleagues at the main campus and across the Network and identify best treatments and clinical trials for individual patients. We are also utilizing Yale’s molecular profiling expertise to identify specific gene mutations in our patients’ tumors and subsequently personalize their treatment with targeted therapies. This is already helping many of my patients from Hartford and Enfield. In addition, we are working to open clinical trials at our Saint Francis Campus in Hartford to provide easy access to new therapies for our patients.

### Your clinical focus is on the care of patients with gastrointestinal cancers. What new therapies and trials do you have to offer your patients?

There are many clinical trials for patients with gastrointestinal cancers. We have very exciting immunotherapy trials available for patients with gastric, colon, liver, and pancreatic cancer. Immunotherapy has changed the paradigm of cancer treatment and Yale Cancer Center is at the forefront of developing new immunotherapies for our patients. In addition, we also have a very important clinical trial available for colon cancer prevention.

### How do you align your clinical care with the research efforts at Yale Cancer Center?

As we embrace the Smilow pillar of “Closer to Free,” alignment between clinical care and research becomes necessary. In our clinic, while we take care of patients, our focus is to provide best possible treatment and improve cancer care. If you review the NCCN guidelines, for many patients the best recommended treatment is a clinical trial. So when I am at the main campus in New Haven working with the research teams, the focus remains the same. One cannot provide good cancer care without aligning oneself with research. The collaboration between Saint Francis Hospital and Smilow Cancer Hospital has made this connection possible.

Register today at [rideclostofree.org](http://rideclostofree.org)



If you're looking for Connecticut's best ride, you just found it! The **Closer to Free Ride** is on **September 10, 2016**. This year, riders have a new 10-mile option in addition to the Ride's 25, 62.5 and 100-mile routes. One hundred percent of the funds raised by riders and volunteers benefit care and research at Smilow Cancer Hospital and Yale Cancer Center. From the stirring opening ceremony, to the fully supported scenic routes, to the triumphant finish line at the Yale Bowl, the Ride provides inspiration at every turn. **THIS IS YOUR RIDE.**

**A Ride**  
for Smilow Cancer Hospital  
at Yale-New Haven

