

IN-DEPTH

CANCER
RESEARCH



Changing the Cancer Conversation

New approaches, therapies and surgical advances are paving the way for treatment breakthroughs and higher survival rates. **BY AMY PATUREL**

As chronic diseases go, cancer is a behemoth. According to the National Cancer Institute, the annual death toll from cancer in the United States hovers around 600,000 for adults and 2,000 for children and adolescents. Sure, the aging population

is partly responsible for the adult statistics, but there's no denying that cancer takes far too many lives in this country. And sadly, treatments haven't always given patients much bang for their buck. Not only do most therapies come with side effects ranging from nausea to hair loss, but the very treatments doctors prescribe to save patients' lives

can actually place them at greater risk of dying from, you guessed it, cancer.

"We've discovered that a lot of these cancer pathways have multiple side streets," says David Chan, M.D., the oncology director of Torrance Memorial Medical Center in Torrance, California. "So blocking the freeway isn't the end of the

story. The cancer takes an off ramp and keeps growing.”

But the tide may be changing. As a result of the billions spent on cancer research, scientists are beginning to unlock the reasons why a cure for cancer has been so elusive—and in some cases they’re learning how to stop cancer in the process. In fact, some very influential Americans, both within the cancer space and outside of it, believe we’re finally primed to attack cancers in a way that doesn’t just extend lives for mere months, but essentially eradicates the disease entirely.

One standout example: Last year, Vice President Joe Biden said that with a new “moonshot,” America can cure cancer. The term pays homage to President John F. Kennedy’s 1962 speech, which convinced Americans that if we put ourselves to the task, we could land on the moon. To drive cancer research forward, in February President Obama tasked Biden with leading the Cancer Moonshot Task Force, the priorities of which include committing to give scientists at the National Institutes of Health the biggest budget they’ve had in more than a decade.

Thought leaders from the private sector are also throwing their cash into the ring. In April, philanthropist, Napster co-founder and former Silicon Valley mogul Sean Parker created The Parker Institute for Cancer Immunotherapy with a \$250 million effort that brings together the nation’s most prominent cancer researchers to accelerate the development of lifesaving therapies.

“We’re on a trajectory to label this as the golden era for cancer research and treatment,” says Ronald A. DePinho, M.D., president of MD Anderson Cancer Center. “An enormous amount of research has revealed the deepest mysteries of cancer and put us in a position to develop effective preventive strate-



CLOCKWISE FROM TOP: Dr. Karen Godette with a patient at Emory University Hospital Midtown in Atlanta; University of Texas MD Anderson Cancer Center in Houston; MD Anderson lab.

gies, transformative early detection strategies and definitive curative strategies.”

Americans need to step up to the plate as well, particularly since up to 50 percent of cancer deaths are related to preventable causes. Lung cancer is a classic example: Scientists largely know what causes it and they know how to prevent it, yet people continue to smoke. According to the NCI, lung cancer claims more lives than the next three most common cancers (colon, breast and prostate) combined.

Packing on extra pounds plays a role in cancer, too, yet two-thirds of Americans are overweight or

obese. A growing body of research suggests that diets high in fruits and vegetables may reduce risk and that loading up on red meat, saturated fats and dairy products may boost risk. More recently, studies have linked sugar to an increased risk of breast cancer. “Change the American diet and lifestyle and you’ll dramatically reduce the incidence of cancer in this country,” says Chan.

Reducing cancer mortality is about understanding your risk, eating properly, exercising and not smoking—and it’s about getting colonoscopies, mammograms, Pap smears and other screening

exams so doctors can catch cancers early when the chance of a cure is greatest. And as Americans are encouraged to boost their own odds, researchers and doctors are working tirelessly to find new ways to combat cancer.

IMMUNOTHERAPY BREAKTHROUGHS

Dating back to the early 1900s, scientists predicted rousing the immune system would be the silver bullet for cancer treatment. Studies on rodents in the 1960s showed that immune responses could effectively eliminate tumors, but replicating the findings in human cancers repeatedly failed.

It seemed the immune system was asleep at the wheel with cancer. No one understood why bolstering immunity didn't work, and the concept of immunotherapy became a sort of snake oil. But James P. Allison, Ph.D., chair of Immunology at MD Anderson Cancer Center, wasn't thwarted.

"I had this idea that if we could understand how to turn the immune response on and off, we had a fighting chance to cure cancer," he explains. The immune system not only employs an army of killer T cells (the immune system's primary attack cells) that can be reawakened if a tumor recurs, but they can also adapt along with the tumor.

Trouble is, cancer cells are so adept at hiding that the immune system often needs a homing beacon to sound an alarm to the T cells. In 1982, Allison identified and elucidated the structure of something called the T cell antigen receptor.

"The T cell antigen acts almost like an ignition switch for the immune system," explains Allison. But it wasn't enough to drive the immune system by itself. So several years later, scientists discovered two molecules—CD28 and CD24—that serve as secondary stimulation signals.

"IF WE STUDY WHY SOME PATIENTS RESPOND AND OTHERS DON'T, WE CAN MAKE PROGRESS IN TERMS OF COMBINING IMMUNOTHERAPY WITH OTHER DRUGS AND TREATMENTS TO GET BETTER RESULTS."

—ANTONI RIBAS, M.D., PH.D., PROFESSOR OF MEDICINE AT UCLA AND DIRECTOR OF THE TUMOR IMMUNOLOGY PROGRAM AT THE JONSSON COMPREHENSIVE CANCER CENTER.

But as soon as you start the ignition and step on the gas, you also engage the genes that put on the brakes, so you only have a certain amount of time to run until the system turns off. "Otherwise, immune cells continue dividing ultimately destroying healthy cells," says Allison. "So I thought, let's just disable the brakes for a time and unleash the immune system to attack the cancer."

That's when Allison discovered how to block CTLA-4, a crucial molecule that stops the immune system's normal attack, enabling cancer cells to invade tissue. His thought: Block the molecule with an antibody, a mechanism he describes as a "checkpoint blockade," and free up the T cells to fight back.

The results were astonishing. When Allison's team did their first checkpoint blockade experiments in mice, the tumors melted away. Human studies, too, were impressive. Long-term follow up of 5,000 patients with metastatic melanoma—a deadly disease with a median survival rate of 11 months—shows that nearly one-quarter of those who took a checkpoint therapy called Ipilimumab (or Yervoy) survived for 10 years.

"That's what is so exciting about the checkpoint approach," says Antoni Ribas, M.D. and Ph.D., professor of medicine at UCLA and director of the Tumor Immunology Program at the Jonsson Comprehensive Cancer Center, who has been actively involved

in immunotherapy research and expediting its delivery to patients. "When it works, it usually works for a long time—complete remission or disease so tamped down that life returns to normal for patients who once faced certain death."

Allison cites a patient he met in 1996, a woman in her mid-20s who had just finished college and was newly married—and hospice-bound with metastatic melanoma. "She had been treated with Yervoy and when I met her one year later, her tumors were gone," says Allison. "Meeting her along with her husband and parents was quite emotional. A few years later, she sent

IMMUNOTHERAPY SIDE EFFECTS

For some patients, immunotherapy comes with significant side effects, but "it's not like chemotherapy where you know your hair is going to fall out or your skin is going to slough off," says James P. Allison of MD Anderson Cancer Center. Nevertheless, doctors monitor patients closely, applying certain algorithms to treat patients who experience adverse effects. In some cases, patients require potent antiinflammatory drugs to prevent the inflammation that accompanies an immune system on the attack.

me a photo of her first child. Then a couple of years after that, she sent me a photo of her second child.” Two decades later, the two are still in touch and she’s doing great.

For Allison, who is a prostate cancer and melanoma survivor himself and whose mother, brother and two uncles died from cancer, it feels good to deliver a blow to a disease that causes such devastation. But the work is far from over. One of the important mysteries researchers still have to solve is why the treatment doesn’t work for more patients.

“If we study why some patients respond and others don’t, we can make progress in terms of combining immunotherapy with other drugs and treatments to get better results,” says Ribas.

Since Yervoy, researchers have uncovered other immune checkpoint and secondary stimulation molecules and new drugs are advancing through clinical trials. Two drugs of this type have already won FDA approval—and Yervoy is showing promising results with other cancers, including kidney cancer, lung cancer, head and neck cancer and bladder cancer.

“We’re seeing spectacular cures in a substantial number of people,” says Allison. “We know it works . . . we just have to keep working on it.”

ADOPTIVE T CELL THERAPY

With immunotherapy, checkpoint blockades unleash the immune system to attack cancer. Unfortunately, for the approach to work, the T cells have to be preexisting in the tumor—or in the patient. But scientists across the country are finding ways to work around this obstacle by genetically modifying T cells to spot and kill cancer.

The process, called chimeric antigen receptor therapy, or CAR T-cell therapy, has produced dramatic responses in leukemia and lymphoma patients. In fact, in early trials



MD Anderson Cancer Center

“WE’RE ON A TRAJECTORY TO LABEL THIS AS THE GOLDEN ERA FOR CANCER RESEARCH AND TREATMENT.”

— RONALD A. DEPINHO, M.D., PRESIDENT OF THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER IN HOUSTON

of patients with advanced acute lymphoblastic leukemia who had few remaining treatment options, many of their cancers have disappeared entirely.

According to Ribas, CAR T-cell therapy acts almost like a GPS system, redirecting the patient’s immune system to a target that’s unique in the cancer while sparing normal cells. So far, a marker for leukemia and lymphoma called CD19 is the most successful target the therapy has been able to track.

“CD19 is really the poster child for this type of therapy,” says Stephen J. Forman, M.D., director of the T cell Immunotherapy Research Laboratory, and Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation, at City of Hope National Medical Center in Duarte,

California. “We are working hard to identify other targets and engineer T cells to recognize them so we can expand CAR T-cell therapy to effectively attack other cancers, including brain, liver and prostate cancers.”

In other experiments, scientists are using something called adoptive T cell therapy to harness the power of T cells that have tried to attack the tumor but failed. One way to do this is to grow cells called tumor-infiltrating lymphocytes, or TILs, to several billion in the lab, and then reinfuse them into the patient in an attempt to overwhelm the tumor.

“The hope is that these highly specific, specialized populations of T cells will seek and destroy the tumor and remain as memory cells to protect against recurrence,” explains Cassian Yee, Professor,

Department of Melanoma Medical Oncology at MD Anderson Cancer Center.

The approach has proven effective in patients with certain forms of leukemia and metastatic melanoma, producing in some patients a complete, long-lasting response. It's also showing promise in fighting prostate, lung, breast, ovarian, pancreatic and colon cancers.

“The future of immunotherapy will be to develop combination strategies that bring together adoptive therapy, cancer vaccines, immune checkpoint inhibitors, radiation therapy and other modalities to thwart immune escape mechanisms and defeat cancer,” says Yee.

VACCINE DEVELOPMENT

Experts agree that vaccination is the single most important public health initiative in modern history. The gist: You receive an injection

“WITH DIAGNOSTIC IMAGING RAPIDLY ADVANCING, DOCTORS ARE OFTEN ABLE TO FIND CANCER EARLIER NOW THAN THEY WERE DECADES AGO.”

— SADIA KHAN, D.O., BREAST SURGICAL ONCOLOGIST AND ONCOPLASTIC SURGEON AT HOAG MEMORIAL HOSPITAL PRESBYTERIAN IN ORANGE COUNTY, CALIFORNIA

with an innocuous form of the virus that teaches your immune system to develop antibodies and effectively fight future infection.

Until recently, vaccinating against cancer appeared to be a losing battle. Unlike viruses, cancer cells can sometimes sport the same molecules as normal cells. As a result, revving up the immune system to target common cancer molecules hasn't worked.

So, scientists focused their efforts on developing vaccinations for viruses that can trigger cancer, including hepatitis B (one of the

leading causes of liver cancer) and human papillomavirus, a type of virus that causes 99.7 percent of cervical cancers and affects up to 90 percent of the population.

Since it arrived on the market in 2006, the HPV vaccine has helped reduce the prevalence of cervical cancer by a whopping 64 percent in girls 14 to 19 years and by 34 percent among those 20 to 24 years old, according to a study published in the journal *Pediatrics*.

“It has exceeded everyone's expectations,” says Lauri Markowitz, M.D., medical epidemiologist at

HOW CANCER RESEARCH HAPPENS

THERE ARE A LOT OF STEPS—AND OFTEN SEVERAL YEARS, EVEN DECADES—FROM IDEA TO IMPLEMENTATION IN THE CANCER-RESEARCH WORLD.

Cancer research starts with an idea. It could be something as simple as exploring whether eating fruits and vegetables lowers cancer risk. Or as complex as mapping the Cancer Genome Atlas, a comprehensive effort to catalog the genetic mutations that cause cancer.

Laboratory research (aka “bench science”) is the foundation for solving real-world problems. Clinical trials allow scientists to study how these basic research findings perform in humans. Translational research helps

ensure that findings make it from the lab to the bedside. And observational research helps scientists develop theories about potential causes of cancer and suggest possible preventive measures.

Unfortunately, translating lab-rat research into real-world advances is often agonizingly slow. Each of these investigative areas involve years of work, in some cases decades.

MD Anderson's James P. Allison's checkpoint blockade research is a classic example. He has devoted his life's work to

understanding how the immune system operates and developing strategies for using the immune system to attack cancer. His first lab discovery relating to immunotherapy occurred in 1982. The FDA approved the first checkpoint blockade drug Ipilimumab (Yervoy) more than three decades later, in 2011.

Even once a drug such as Yervoy makes it to late-phase clinical trials, patients must be followed for several years, or even decades, before the FDA can deem a new treatment safe and effective. Similarly, with

population-based research, studies typically follow groups of people through interviews, surveys, medical records and a myriad other means for several years.

So, yes, cancer research is a marathon, not a sprint. But researchers across many different disciplines—and even influential thought leaders in other sectors—believe that the marathon is gaining speed as scientists move toward pivotal research discoveries that will forever change the cancer conversation.



CLOCKWISE FROM TOP:
California's Torrance
Memorial Medical Center;
TMMC Oncology Director
Dr. David Chan; Cancer
treatments at TMMC.

the National Center for Immunization and Respiratory Diseases at the Centers for Disease Control and Prevention. In addition to gynecological cancers, the vaccine protects against HPV types that can cause cancers of the back of throat, penis and anus.

Despite these promising results, only about 40 percent of adolescent girls and 60 percent of adolescent boys receive proper vaccination, according to the CDC. According to a 2014 study published in the journal *Sexually Transmitted Diseases*, more than a third of parents in the United States don't know the vaccine exists. And while there has been a recent spike in vaccine uptake among adolescent boys, receipt of any dose of HPV vaccines among adolescent boys still remains low. In fact, many parents are unaware

that HPV vaccines should be given to boys. There's also a subset of the population that believes delivering the HPV vaccine promotes sexual promiscuity, even with evidence to the contrary, says DePinho.

"When the hep B vaccination was first licensed, it was targeted to health care workers and high-risk groups and also had a hard time gaining widespread acceptance," says Markowitz. "Eventually, though, it became part of the infant vaccination schedule."

Research continues to suggest that the immune system is cancer's most powerful foe. In 2010, the FDA approved the first cancer treatment vaccine using patients' own immune cells to protect against metastatic prostate cancer that no longer responds to hormone therapy. And trials are underway

to uncover whether a vaccine can prevent breast cancer recurrence.

There's even a recent push to combine vaccines with chemotherapy and other treatments among patients with established diseases. Among women who have late-stage cervical cancer, for example, preliminary data suggests combining the HPV vaccine with chemotherapy could help boost the body's immune response to fight the disease.

"Combination strategies that use one agent such as a vaccine to stimulate a T cell response prior to administering a checkpoint blockade to take the brakes off that T cell response may prove to be more efficacious than either approach alone," says Elizabeth Mittendorf, M.D., Ph.D., associate professor in the Department of Breast Surgical Oncology at MD Anderson Cancer Center.

SURGICAL ADVANCES

Surgery will always be a critical weapon in the battle against cancer. And today's patients have a distinct advantage over previous generations.

"With diagnostic imaging rapidly advancing, doctors are often able to find cancer earlier now than they were decades ago," says Sadia Khan, D.O., breast surgical oncologist and oncoplastic surgeon at Hoag Memorial Hospital Presbyterian in Orange County, California. Couple that with newer surgical techniques, and some patients may be able to escape invasive surgery.

Rather than commit to weeks of radiation to effectively eliminate cancer and prevent recurrence, select breast cancer patients can now opt to receive a one-time therapy called intraoperative radiation therapy, or IORT.

While radiation oncologists have used IORT for decades in gastrointestinal and soft-tissue cancers, it has always been part of

a suite of treatments. “Now with breast cancer, we’re using IORT as a definitive treatment” for early stage breast cancer in carefully selected patients, says Karen Godette, M.D., medical director of the Winship Cancer Institute’s Radiation Oncology Department at Emory University Hospital Midtown in Atlanta.

After removing the lump surgically, doctors use an applicator to temporarily insert a balloon into the same (tiny) incision with a low-energy x-ray machine that deliv-

ers a single fraction of radiation, reducing the amount of harmful radiation exposure. The treatment usually lasts between eight and 12 minutes. Then doctors remove the balloon, close the incision and patients are able to go home the same day.

According to Godette, many women choose to have a total mastectomy because they live too far away to get weekly radiation treatments, they are afraid of the toxicity of the treatments, they

don’t have transportation or can’t afford to miss work and family obligations. With IORT, women can sidestep those issues and save their breasts in the process.

One of the pillars of advanced ovarian cancer treatment is completely removing all visible tumors—an achievement strongly tied to survival. Researchers at MD Anderson Cancer Center have implemented an algorithm to increase their ability to achieve that end.

While a combination of surgery

MINDING CANCER

PSYCHOLOGICAL ONCOLOGY ISN’T NEW, BUT IT’S BECOMING MORE COMMONPLACE. THIS APPROACH COMPLEMENTS MORE TRADITIONAL TREATMENTS, ENHANCING IMMUNITY AND LOWERING STRESS LEVELS IN PATIENTS.

Advanced cancer doesn’t just have physical effects. It threatens to rob patients of their identities, livelihoods and even their relationships. The emotional toll of cancer—or even of a genetic predisposition to developing cancer—is huge.

Psychosocial oncology works alongside conventional medicine to support the body’s ability to fight cancer by reducing stress levels, enhancing immunity and modulating nervous system activity. While this may sound like a soft approach for a tough disease, it’s backed by hard science. As a result, a growing number of cancer centers are incorporating a smorgasbord of supportive care programs into their treatment efforts. Here, a sampling of the psychosocial oncology efforts cropping up at cancer centers across the country:

SUPPORT GROUPS: Dating back to 1989, researchers discovered that women with metastatic breast cancer who participated in a year of weekly group therapy sessions had an 18-month survival advantage over those who navigated their cancer journey without that support.

WRITING PROGRAMS: At Memorial Sloan Kettering Cancer Center, nearly 1,200 patients have found solace in

the written word through a unique program called Visible Ink. The program matches patients with a professional writing mentor to help them explore their thoughts and emotions on the page.

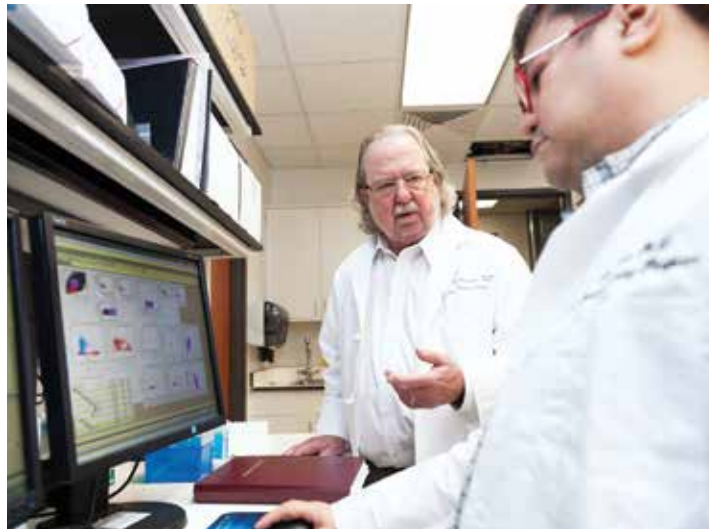
IMAGE SERVICES: In addition to the physical and emotional toll, cancer affects patients’ appearances—whether that means loss of their breasts or hair, or surgical scars. At City of Hope in Duarte, California,

the American Cancer Society sponsors a program called Look Good Feel Better to help patients look and feel more like themselves as they navigate the physical changes that accompany common cancer treatments.

END-OF-LIFE CARE: At cancer centers across the country, including Dana-Farber Cancer Institute in Boston, professional counselors facilitate conversations about end-of-life issues and help families prepare for pain management, hospice and managing logistical matters related to death. The irony: Studies show such tactics actually have some survival benefits. A study published in the *New England Journal of Medicine*, for example, reported that lung cancer patients who received an average of four visits with a specialist to discuss resuscitation preferences, pain control and quality of life

lived almost three months longer than those who received standard care.

LEGACY SERVICES: When treatment options have been exhausted and patients are nearing death, supportive care increasingly involves helping them focus on their legacy by directing them to services such as LifeChronicles, a nonprofit organization that offers documentary-style videos for terminal patients, free of charge. For the spouses, children and siblings left behind, personal documentaries help them remember what it felt like to be with the person. Preliminary studies even suggest these videos reduce stress and anxiety among the survivors. “The experience can be something families draw on for comfort and peace. And they can play it repeatedly,” says LifeChronicles founder Kate Carter.



FROM LEFT: Dr. Ronald A. DePinho at MD Anderson Children's Cancer Hospital; MD Anderson Cancer Center doctors in the lab.

“THE FUTURE OF IMMUNOTHERAPY WILL BE TO DEVELOP COMBINATION STRATEGIES THAT BRING TOGETHER ADOPTIVE THERAPY, [VACCINES], IMMUNE CHECKPOINT INHIBITORS, RADIATION THERAPY AND OTHER MODALITIES TO THWART IMMUNE ESCAPE MECHANISMS AND DEFEAT CANCER.”

— **CASSIAN YEE, PROFESSOR, DEPARTMENT OF MELANOMA MEDICAL ONCOLOGY AT MD ANDERSON CANCER CENTER**

and chemotherapy is still the gold standard treatment for patients with advanced ovarian cancer, the sequence of therapies varies among clinicians. And some specialists believe the choice can dramatically impact survival rates. According to Anil K. Sood, M.D., professor in the Department of Gynecologic Oncology & Reproductive Medicine at MD Anderson Cancer Center, applying this algorithm, which requires laparoscopic investigation, makes the decision more clear-cut.

Here's how it works: During laparoscopy, surgeons score the extent of spreading cancer based on specific parameters. According to the MD Anderson algorithm, patients with a score less than 8 get surgery first while those with a score of 8 or higher undergo three to

four cycles of chemotherapy prior to surgery.

Prior to the algorithm, “if you operate on everyone up front, with a big incision, even in experienced hands, complete tumor removal is only achieved 20 to 30 percent of the time,” says Sood. By implementing the new algorithm, doctors have boosted that rate to almost 90 percent among those treated with surgery before chemotherapy and to 80 percent for patients who undergo chemotherapy prior to surgery.

While it's still too soon to tell how the algorithm will impact survival rates, Sood believes it's an important milestone in terms of delivering better and more personalized care to patients with advanced ovarian cancer.

Removing a disease-riddled

prostate is still commonplace for men with newly diagnosed prostate cancer. But with better screening methodology and increased awareness, doctors are detecting prostate cancers at an earlier stage when removing the entire prostate (which carries significant risks of impotence and incontinence) may not be necessary.

In fact, a handful of doctors across the country are performing focal laser ablation, a procedure that relies on magnetic resonance imaging to guide a laser fiber directly into the tumor and burn it. The MRI-guided laser can ablate with precision right up to the edge of the prostate, preserving the delicate neurovascular bundle (responsible for erectile function) that runs within millimeters of the prostate and is often damaged during a prostatectomy. “The laser we use is like a scalpel that, in the hands of a skilled practitioner, can ablate right up to the nerves with low risk of damaging them,” says Ara Karamanian, M.D., medical director of the Prostate Laser Center in Houston. Plus, with focal laser ablation,



Ara
Karamanian,
M.D.

“THE LASER WE USE IS LIKE A SCALPEL THAT, IN THE HANDS OF A SKILLED PRACTITIONER, CAN ABLATE RIGHT UP TO THE NERVES WITH LOW RISK OF DAMAGING THEM.”

— ARA KARAMANIAN, M.D.,
MEDICAL DIRECTOR OF THE PROSTATE LASER CENTER

patients go home within hours and typically require only a few days of recovery time compared to a one- to four-day hospital stay for conventional prostatectomy—even if the surgeon uses a minimally invasive approach.

The caveat: Such approaches require expensive and advanced equipment, not to mention highly skilled physicians with expertise in a technique that isn't yet covered by insurance. Even the leading cancer centers may not offer these technologies, so patients are forced to pay \$20,000 to \$30,000 out of pocket at standalone clinics.

A better approach for men with slow-growing prostate cancer may be to skip treatment entirely. A study published in the *New England Journal of Medicine*, for example, found that prostatectomy among men with localized prostate cancer didn't affect life expectancy.

Instead, patients may embark on a protocol called “active surveillance,” where physicians monitor the disease with prostate-specific antigen tests, periodic biopsies and other exams to ensure the disease hasn't significantly progressed. Experts agree that the vast majority of men with prostate cancer are never going to be symptomatic or die from their cancer, so why should they risk impotence or incontinence?

SPOTLIGHT: MULTIPLE MYELOMA

Two or three decades ago, a multiple myeloma diagnosis was a death sentence. A cancer of plasma cells that live in the bone marrow,

multiple myeloma diminishes the body's ability to make antibodies and fight disease. As the cancerous cells build up in the bone marrow, they usually form tumors in the bones and soft tissue. They also displace healthy red and white blood cells and thicken the blood, possibly leading to bone fractures, kidney problems, even fatal infections.

But the disease often comes on with little to no warning, explains Gareth Morgan, M.D., Ph.D., director of the Myeloma Institute at the University of Arkansas for Medical Sciences in Little Rock. The first sign for many patients is a bone fracture, pain from a bone fracture or back pain.

“They can develop pain in their hip or back, spike a fever and go into renal failure,” says Morgan.

Historically, doctors treated multiple myeloma with high-dose chemotherapy followed by a stem cell transplant—a grueling procedure similar to a blood transfusion. Despite these titanic efforts, the “incurable cancer” often returns.

In the past few years, the multiple myeloma landscape has changed dramatically. With early detection capabilities, immune-boosting agents and combination therapies, the average multiple myeloma patient can expect to live six to 10, or more, years after diagnosis, compared to just two to three years a decade ago. In fact, multiple myeloma patients diagnosed today may not even die from the disease.

“Compared to other cancers, we've made huge progress—up to 60

percent of people with a previously fatal disease are alive and well 15 to 20 years after diagnosis,” says Morgan. “With the age distribution for this disease, that equates to a cure.”

This radical shift toward the other “c-word”—cure—evolved from scientists gaining a new understanding of how myeloma cells interact with surrounding cells and tissues. They hatched ways to interfere with the cancer process—blocking myeloma cells' access to nutrients and jamming signals that promote cell growth—and paved the way for a cadre of new treatments to address this complex cancer, including three drugs that won FDA approval in November 2015. Among the standouts: **Proteasome inhibitors:** These agents, including Kyprolis (carfilzomib), Velcade (bortezomib) and Ninlaro (ixazomib), interfere with the protein destruction required for myeloma cells to grow. Like a plug in a garbage disposal, proteasome inhibitors prevent the destruction of myeloma cells' unwanted proteins.

“Without that garbage disposal, the myeloma cells become saturated with unwanted proteins, go into metabolic paralysis and die,” says Ruben Niesvizky, M.D., director of the Multiple Myeloma Center at Weill Cornell Medicine and New York-Presbyterian in New York City. **Immune system modulators:** IMiDs including Thalomid (thalidomide), Revlimid (lenalidomide) and Pomalyst (pomalidomide), starve myeloma cells by cutting off their blood supply while at the same time

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Jorge Oviedo.

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Adventurer: Jorge Oviedo (Paragliding Medellín, El Rancherito & Mahalo).

Romantic: Simon Willis (Diez Hotel & Museo El Castillo); Jorge Oviedo (Alambique & Dancefree).

Arts Aficionado: Jorge Oviedo (Café de Otraparte & Museo de Arte Moderno).

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Alaire libre: Michael Weber (The Pottinger); Justin Lim (Sohofama); Pisaphotography/Shutterstock.com (Aqua Luna Harbour Discovery Tour)

rousing the body's disease-fighting T cells.

Antibodies: Like a homing beacon for cancer cells, anti-CD38 monoclonal antibodies bind to a target on the myeloma cell that signals the patient's immune cells to attack and eliminate myeloma cells.

According to Morgan, the growing number of options within each of these drug categories represents hope for patients who have relapsed on standard therapies. Today, doctors are even using triplet therapies (three agents of various kinds) to attack the disease from all angles. So a doctor might use one proteasome inhibitor, one immune system modulator and one steroid to simultaneously fight the disease and bolster the immune system's defense.

"Each of these agents have borderline activity against multiple myeloma by themselves. When combined with other therapeutics, we're seeing overall responses of more than 90 percent," says Niesvizky. "The responses are so deep and durable that they're becoming the rule rather than the exception."

Of course, each medication comes with its own set of side effects, including neuropathy (numbness and tingling in the hands and feet), nausea and fatigue, but newer-generation drugs don't carry the same risks of toxicity. And using established drugs in new combinations not only reduces toxic side effects but also enhances long-term survival.

"With myeloma we don't have the luxury of targeting one gene like with other cancers. We can't yet do precision medicine, so that's a real challenge. However, we can target myeloma cells by using antibodies, or interfering with their metabolic pathways, to help the immune system fight the cancer," says Niesvizky. "Using the proper combination of agents, we're optimistic we can eradicate the disease entirely." ▾

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DRAWING SAMPLE BEFORE TREATMENT



DRAWING SAMPLE AFTER TREATMENT

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