

# CANCER TREATMENT OPTIONS



*As cancer deaths continue to decline in the United States, more Americans are now surviving cancer than ever before.*

IN 1971, PRESIDENT RICHARD NIXON LAUNCHED A WAR ON CANCER, A GROUP OF MORE THAN 100 DISEASES CHARACTERIZED BY UNCONTROLLED GROWTH AND SPREAD OF ABNORMAL CELLS. IN HIS STATE OF THE UNION ADDRESS, HE CALLED FOR \$100 MILLION IN FUNDING TO FIND A CURE. CONGRESS RESPONDED BY CREATING THE NATIONAL CANCER ACT TO SUPPORT BASIC RESEARCH AND CLINICAL TRIALS. ALTHOUGH A CURE HAS YET TO BE FOUND, NEW SCREENING TOOLS FOR BREAST, PROSTATE AND OTHER CANCERS ARE HELPING TO

IDENTIFY MALIGNANCIES IN THEIR EARLIEST STAGES, WHEN THEY ARE THE MOST CURABLE. ARMED WITH NEW KNOWLEDGE ABOUT THE GENETICS OF CANCER CELLS, PHYSICIANS ARE DEVELOPING TARGETED THERAPIES. AS A RESULT OF THIS PROGRESS, CANCER DEATHS ARE DECLINING IN THE UNITED STATES. THERE ARE NOW 10 MILLION AMERICAN CANCER SURVIVORS ALIVE FIVE YEARS AFTER THEIR DIAGNOSIS. IN THIS SECTION, YOU WILL LEARN ABOUT THE LATEST BREAKTHROUGHS AND PROMISING TREATMENTS IN THE PIPELINE.

## NEW HOPE FOR PATIENTS WITH ADVANCED KIDNEY CANCERS

**CANCER RESEARCHERS** have made little progress in the management of advanced kidney cancer since

the 1980's. But that's beginning to change, thanks to the development of new targeted therapies that are bringing hope to the estimated 54,400 Americans who will be diagnosed with kidney cancer this year.

"Kidney cancer is a difficult malignancy to treat because it usually produces no symptoms in the early stages," says Dr. Robert J. Motzer, an attending physician at Memorial Sloan-Kettering Cancer Center (MSKCC) in Manhattan. "Most kidney tumors are discovered when patients are being evaluated with radiologic imaging studies for non-specific abdominal complaints or during follow-up for other previously treated malignancies. By the time kidney tumors are diagnosed, they are often quite large and have spread to other organs."

Surgery is the most common form of treatment for kidney tumors. Although it is often the only treatment necessary, some patients require additional treatment with chemotherapy if kidney cancer cells have spread to other parts of the body. "The recent development of transduction inhibitor drugs has helped many patients with clear-cell kidney cancers — the most common type of kidney tumor — who have not responded well to traditional chemotherapy," says Dr. Motzer.

“Unfortunately, however, some patients also don’t respond to transduction inhibitor drugs like Sutent [sunitinib malate] and Nexavar [sorafenib].”

To help these patients, Dr. Motzer and a team of research at MSKCC recently completed a study of a new experimental targeted therapy known as everolimus. Dr. Motzer presented data from an international multicenter phase III clinical trial at a meeting of the American Society for Clinical Oncology May 31. The data showed that everolimus significantly delayed cancer progression in patients whose disease had progressed while they had been taking Sutent and/or Nexavar. “Everolimus is an important advance because it targets a different molecular pathway than the other drugs,” says Dr. Motzer. “It interferes with the mTOR protein, which acts as a central regulator of tumor cell division,

cell metabolism and blood vessel growth.” Another advantage, says Dr. Motzer, is that everolimus is a pill that is taken once a day, which makes it more convenient for patients.

More than 400 patients participated in the phase 3 clinical trial. After 6 months, tumors had not grown or spread for 26 percent of patients who had received everolimus compared to only 2 percent of patients receiving placebo. The average progression free survival was 4 months for patients taking everolimus, compared to 1.9 months for patients receiving placebo. Because of these positive

### EVEROLIMUS HALTS DISEASE PROGRESSION BY TARGETING A DIFFERENT MOLECULAR PATHWAY THAN OTHER DRUGS.

interim results, an independent monitoring committee halted the trial in February 2008, allowing researchers to offer everolimus to the group receiving placebo.

The Lancet, a British medical journal, in its Aug. 9-15, 2008 issue that cited the study says: “Everolimus should now be regarded as the standard-of-care-for patients with metastatic renal cell carcinoma whose disease has progressed after treatment with targeted therapies.” Says Dr. Motzer, “Other research will be done to determine whether everolimus can be used to treat lymphoma and neuroendocrine tumors, We also hope to come up with other new drugs, so that kidney cancer can be managed as a chronic disease.”

## SURGICAL ROBOTS USED TO TREAT PROSTATE CANCER

**THE AMERICAN CANCER SOCIETY (ACS) estimates that in 2008 about 186,320 men will receive the bad news that they have prostate cancer.** About one in six men will be diagnosed with prostate cancer during his lifetime, making it the most common cancer in American men other than skin malignancy. The good news, however, is that only one in 35 will die of the malignancy. More than two million men in the US who have been diagnosed with prostate cancer are alive today, and the number is expected to increase. “Technology has made a significant difference,” says Dr. Mani Menon, director of the Vattikuti Urology Institute at Henry Ford Hospital in Detroit. “Not only are more men surviving prostate cancer, but their quality of life after treatment has improved.”

The latest advance is robotic prostatectomy, a high-tech procedure that treats early-stage prostate cancer with the assistance of a surgical robot. For the surgeon, the robotic system offers the advantage of maneuverability and precision in the use of instruments. To ensure satisfactory results, however, surgeons require extensive training and experience, as it is the most challenging technique to master in prostate cancer surgery. The team at Henry Ford has performed more than 4,000 robotic prostatectomy operations, more than any other hospital in the world. Patients from all 50 states and more than two dozen countries have traveled to Michigan for the procedure.

A team of surgeons led by Dr. Menon, Dr.



Today, a greater number of men with prostate cancer are not only surviving the disease but also enjoying significantly improved quality of life than their predecessors.

### Upcoming Seminars Sponsored by Memorial Sloan-Kettering Cancer Center's Post-Treatment Resource Program

#### Urinary Incontinence—Options for Management

Tuesday, Oct. 14, 2008

#### Coping After Cancer: What We've Learned from Survivors

Wednesday, Oct. 29, 2008

#### Colorectal Cancer Treatment and Survivorship: Talk with the Experts

Tuesday, Nov. 18, 2008

#### Managing Chronic Pain

Tuesday, Dec. 9, 2008

Call 212-717-3527 to RSVP. Registration is required. All seminars take place from 5:30 to 7:00 PM in the MSKCC Rockefeller Research Laboratories, 430 East 67 Street (between York and First Avenues), Manhattan.

### Upcoming Memorial Sloan-Kettering Cancer Center's CancerSmart Lecture

#### An Update on Brain and Spinal Cord Cancers

Tuesday, Oct. 21, 2008

Call the CancerSmart infoline at 212-639-3074 to RSVP, or visit [www.cancersmart.org](http://www.cancersmart.org) to register. Registration is preferred. The lecture will take place from 6:00 to 7:30 PM in the MSKCC Rockefeller Research Laboratories, 430 East 67 Street (between York and First Avenues), Manhattan.

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MEMORIAL SLOAN KETTERING

James Peabody and Dr. Hans Stricker perform the minimally invasive surgery using the da Vinci Robotic Surgical System, which includes a robot, miniaturized surgical instruments and a high definition, 3-D computer system. With the da Vinci robot, the surgeon makes five keyhole openings rather than a single six-inch incision used during the traditional “open” prostatectomy. “Smaller incisions mean less pain and faster recoveries,” says Dr. Menon. “Most patients resume their normal activities within one to two weeks. Seven-year-survival rates and quality of life measures show that the robotic prostatectomy is safe and effective.” (Like all medical procedures, robotic prostatectomy isn’t for everyone. Patients must be free of other significant health problems and be within a fairly normal weight range.)

Using the 3-D computer system, the surgeon manipulates the robotic arm, which inserts tiny instruments into the abdomen through the incision. A laparoscope — a long, thin lighted telescope — is also inserted through one incision and connected to the computer monitor. This allows the surgeon to view the prostate and surrounding tissue in precise detail. Sitting at a console, the surgeon precisely transfers his hand, wrist and finger movements to the robotic arm inside the patients in order to remove the cancerous prostate, nearby lymph nodes, seminal vesicle, and adjacent tissue through the small incisions. “The incisions are closed with a few stitches,” says Dr. Menon. “The procedure takes about 2 to 2 ½ hours. Patients have very little pain after surgery; most go home within 24 hours.”

Because the team at Henry Ford is a world leader in the procedure, its results are outstanding. In addition to less blood loss and scarring, patients have better outcomes in sexual function and urinary continence than patients who have the traditional open prostatectomy. When the prostate is removed, one of the two muscles that normally control urination is also removed. The second muscle will compensate for the first muscle over time. Most men who have prostate surgery have mild to moderate urinary leakage that may last from 6 to 12 months, but with the robotic prostatectomy technique, they regain continence much faster. The team also reports significant patient benefit in another key respect. “We have developed a new variation of the robotic prostatectomy called the Veil of Aphrodite that offers added protection to the nerves, which play an important role in penile erections,” says Dr. Menon. “As a result of this technique, many patients have had earlier return of and better quality erections as well as better urinary control.”



*A precipitous rise in melanoma rates among young American women highlights the need for increased education and vigilance.*

## MELANOMA INCREASES AMONG YOUNG WOMEN

**MELANOMA, the most serious form of skin cancer, is increasing among young women according to a study in the July 10 issue of the Journal of Investigative Dermatology.** Researchers at the National Cancer Institute’s Division of Cancer Epidemiology and Genetics found that the number of cases among 15- to 39-year-old white women increased 50 percent from 1980 to 2004.

“These findings are important because they show that we must increase efforts to educate young people about the dangers of melanoma,” says Dr. Anna C. Pavlick, director of the NYU Cancer Institute’s melanoma program at the NYU Langone Medical Center in Manhattan. “Although melanomas make up the smallest percentage of all skin cancers, they cause the greatest number of deaths because they are more likely to spread to other parts of the body.” Exposure to ultraviolet (UV) radiation from sunlight or tanning beds increases the risk. “Young people often feel invincible so they don’t take precautions when they are in the sun, like wearing sunscreen,” she says. “Tanning beds are especially dangerous because they enable young people to get a tan 365 days a year, which increases their risk of melanoma later in life.”

Caucasians are at greatest risk because they have less pigment in their skin to protect against damaging UV radiation. Fair-skinned people who have blond or red hair, light-colored eyes and who freckle or sunburn easily are more likely to develop melanoma than those with darker complexions. “When melanoma occurs in people with dark skin tones, it often occurs in hidden areas such as under a nail,” says Dr. Pavlick. “Melanoma can also develop in the pigment-containing cells of the retina of the eye, the mouth, digestive tract, urinary track or vagina.” Most melanomas are found in areas that have been exposed to the sun, such as the back, legs, arms and face. Soles of the feet and palms of the hands may also be affected.

“The first signs of melanoma are often changes in an existing mole or the develop-

## SUNBATHING AND TANNING BEDS SET STAGE FOR SKIN CANCER LATER IN LIFE.

ment of a new unusual looking growth on the skin,” says Dr. Pavlick. The American Cancer Society (ACS) recommends that people seek medical attention if they notice a new skin

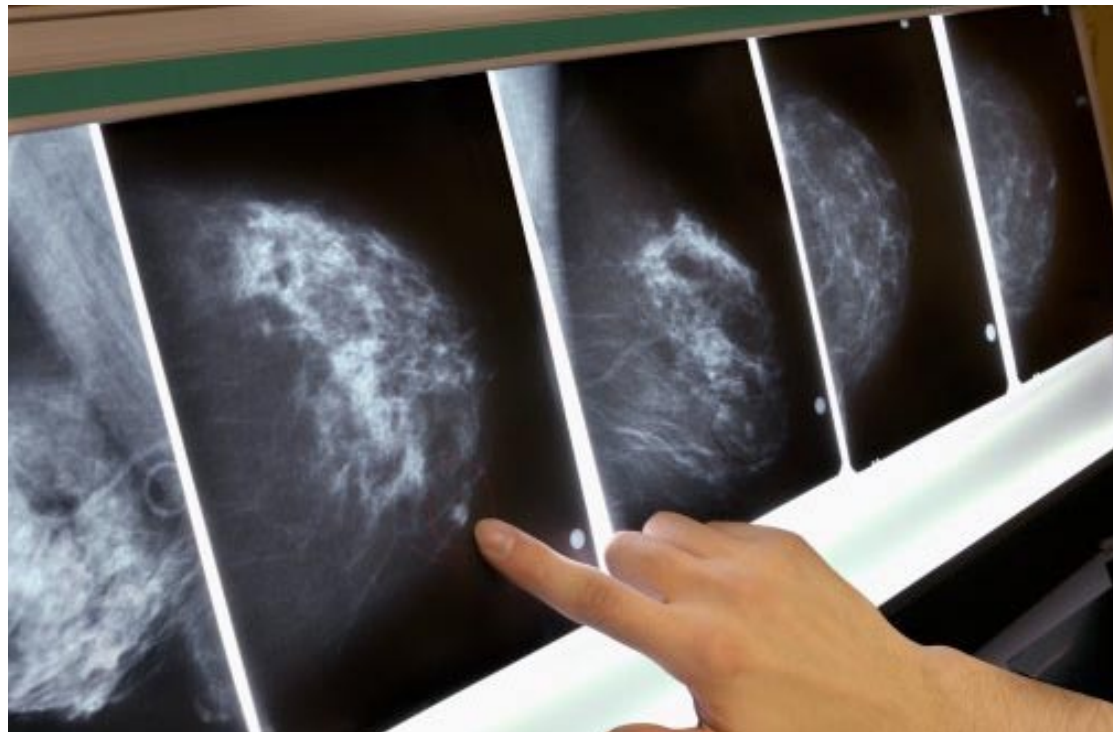
## RHP 5 CHILDREN’S HOSPITAL AND RESEARCH

growth, a change in an existing mole or a sore that doesn't heal in two weeks. The ACS also suggests a complete skin exam every year for people older than 40 and several times a year if the person has a family history of melanoma, numerous moles or other factors that boost risk.

The NYU Langone Medical Center in Manhattan has been one of the world's premier academic medical institutions for more than 167 years. Its NYU Cancer Institute takes a multidisciplinary approach to patient care and features a translational research program that bring together laboratory scientists and clinical research in order to deliver the latest advances in a caring and compassionate setting. More than 20 years ago, NYU dermatologists developed a widely used rule, the ABCD acronym, for recognizing growths that could be early melanomas, and they recently added an E. The warning signs are A (asymmetrical lesions), B (lesions with irregular borders), C (lesions with multiple colors), D (lesions larger than 6 millimeters), and E (evolving lesions that changed in size, color, shape or symptoms over time).

Treatments depend on the stage of the cancer. In general, the thicker the tumor, the more serious the melanoma. Cancers that are confined to the epidermis are easier to treat than those that have traveled beyond the skin. "But even those who have stage 4 — the most serious cancers that have spread to the lungs, liver, and bone — should not give up hope," says Dr. Pavlik. "Although it may not be possible to eliminate the cancer at this stage, there are still many things we can do to ensure that the patient can live a long time and have a good quality of life."

In addition to surgical removal, chemotherapy and radiation therapy may help, as may more recent developments. "Immunotherapies that boost the immune system to help the body fight cancer have made a significant difference," says Dr. Pavlik. "Interferon and interleukin-2 are being used today." Today, clinical trials are underway at NYU Cancer Center to come up with a melanoma vaccine. "Unlike vaccines that are used to prevent other diseases, melanoma vaccines would be used to treat patients with advanced disease," says Dr. Pavlik. "Gene therapies and targeted therapies are also being explored so that melanoma will become a chronic disease like so many other cancers."



*Cutting-edge approaches to the treatment of breast cancer and the follow-up care of breast-cancer patients are saving lives — and women's peace of mind.*

## BREAST CANCER: EARLIER DIAGNOSIS SAVES LIVES, INCREASES TREATMENT OPTIONS

**AFTER BEING DIAGNOSED with breast cancer, the next questions a woman asks are often "Will I survive?" and "How will the malignancy affect my health, appearance and sexuality?"** The good news is that survival rates are increasing: the American Cancer Society (ACS) reports that in 2004 — the latest year for which statistics are available — 2.4 million Americans women had a history of breast cancer. "Thanks to advances in mammography and other detection tools, more breast cancers are being diagnosed in their earliest stages when they are most curable," says Dr. Patrick Borgen, director of breast surgery at Maimonides Medical Center in Brooklyn. "In addition to saving lives, earlier detection gives patients more treatment options." Research in molecular biology has increased knowledge of how breast cancers develop and spread, so that physicians can select and apply the most appropriate treatments, he says.

Maimonides offers a unique program of individualized care that includes a team of breast surgeons, medical oncologists, radiologists and pathologists who can guide patients in assessing their options. Psychological support and other services are also available. "Almost all women with breast cancer will have some type of surgery to remove the cancer," says Dr. Borgen. "In the past mastectomy — removal of the entire breast — was

the only option. But because tumors are now detected in an earlier stage and are often smaller, an increasing number of women are candidates for lumpectomy, removal of only the tumor and some healthy tissue surrounding the tumor to help ensure that all the cancer cells have been removed."

A major difference between the two procedures is that patients who have lumpectomies almost always complete several weeks of radiation to kill any cancer cells left behind in the breast. Patients who have mastectomy don't undergo radiation. In both procedures the lymph nodes under the arm are also examined to determine whether the nodes contain cancer cells, an indication that the cancer has spread there. "The presence of cancer in these nodes is one of the most important factors determining a patient's prognosis," says Dr. Borgen. "Patients with cancer cells require further treatments."

A pioneer in breast surgery, Dr. Borgen uses the sentinel node technique. "In the past, women sometimes developed swelling and discomfort in their arm because a large number of lymph nodes were removed to determine whether the cancer had spread and whether additional treatment would be necessary," he says. "Now we focus on finding the sentinel node — the first node to receive the drainage from breast tissue and, therefore, the first place cancer will travel. If the sentinel node is free of cancer cells, the remaining nodes can be left intact and no further surgery in the armpit will be necessary, which makes the treatment easier for patients."

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MAIMONIDES MEDICAL CENTER

Surgical procedures have been developed to restore the look and feel of the breast after mastectomy. “Having a breast reconstructed helps women feel less self-conscious about how they look and restores confidence in their sexuality,” says Dr. Borgen. “It also helps some women worry less about their health because every day when they get dressed, they are not reminded of the missing breast.” There are two basic types of breast reconstruction. The first uses artificial implants filled with saline or silicone and the second uses skin, fat and muscle from a woman’s own body. Like most medical pro-

## NEW SURGICAL TREATMENTS IMPROVE THE LOOK AND FEEL OF BREASTS

cedures, there are advantages and disadvantages to each. Artificial implants require less extensive operations, says Dr. Borgen, but the results can look and feel less natural than the procedures using a woman’s own tissue.

The surgical team at Maimonides offers the latest techniques in reconstruction. If a patient is having reconstruction immediately after her mastectomy, she may be a candidate for “skin-sparing mastectomy” in which the surgeon removes the inner breast tissue, the nipple, the areola (the dark colored tissue surrounding the nipple), leaving a shell of skin in place. The surgeon then fills in the shell with tissue from the women’s abdomen, and later reconstructs the nipple. “With skin-sparing mastectomy, the reconstructed breast looks and feels like the other breast,” says Dr. Borgen. “Studies show that skin sparing mastectomy is safe and doesn’t increase the risk of recurrence.” The procedure isn’t for everyone, he cautions; patients who have large tumors or tumors that are close to the skin are not good candidates. But for the right patient, the technique is highly effective and produces excellent cosmetic results.

Dr. Borgen predicts that surgical techniques will continue to evolve. “This is a time of great optimism in breast cancer treatment,” he says. “Techniques are improving that not only increase survival but produce a better quality of life after treatment.”

## WOMEN ARE MORE LIKELY TO SURVIVE LUNG CANCER THAN MEN.

**GENDER DIFFERENCES MATTER in lung cancer just like they do in other diseases.** Although lung cancer is the leading cause of cancer deaths among both men and women in the US, women fare better than men who have non-small cell lung cancer, the most common type. In the first study to use surgery, CT and Pet scans to most accurately stage non-small cell lung cancer, University of Alabama at Birmingham (UAB) researchers found that, for stages one through three, the five-year survival rate of women was better than that of men. Overall, 60 percent of women were alive at the 5-year mark, compared to 50 percent of men. For those diagnosed at stage 1, 69 percent of women versus 64 percent of men were alive at 5 years out; in stage two, the rates were 60 percent of women versus 50 percent of men; and at stage 3, the rates were 46 percent of women and 37 percent of men.

“We are not sure why women did better than men in our study of 1,085 patients

between Jan. 1998 and March 2005 at UAB Hospital,” says Dr. Robert J. Cerfolio, chief of thoracic surgery at UAB and lead author of the study, which was published in the Dec. 2007 issue of Chest, a medical journal. “Women may have genetic, biologic and hormonal differences that affect survival.” Further research is needed to determine whether female hormones such as estrogen might affect cancer growth, he says. Genetic differences may also affect the ability of men and women to repair damaged DNA, a factor in the development of cancer.

“One thing we know for certain is that cigarette smoking is the primary cause of lung cancer in both women and men,” says Dr. Cerfolio. “Unfortunately, nearly one-quarter of women smoke, including 500,000 teenage girls, so the incidence of lung cancer in women is catching up to men.” In 2008, the American Cancer Society (ACS) estimates that there will be 114,690 new cases of lung cancer diagnosed in men and 100,330 in women in the US.

“Although lung cancer does occur in non-smokers, [all smokers] should take steps to quit smoking because it is the most important thing to do to reduce risk of lung can-



*Though a UAB study indicates that women with lung cancer have a higher survival rate than their male counterparts, the fact that nearly one-quarter of American women smoke is still cause for great concern.*

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HENRY FORD HEALTH SYSTEM

cer, other serious respiratory conditions like COPD, and heart attacks,” says Dr. Cerfolio. “Avoiding secondhand smoke and exposure to asbestos, radon and other carcinogens is also important.”

Dr. Cerfolio and his team are leaders in lung-cancer surgery, performing more than 1,200 operations a year. Because surgery removes the tumor and nearby lymph nodes, it offers the greatest chance for significant survival for some types of lung cancer, especially those that are early-stage cancers that have not spread to other parts of the body. To help patients recover more quickly, Dr. Cerfolio has developed a new surgical technique that reduces pain. Instead of crushing the intercostal muscle and nerve that lies between the ribs while spreading the rib during a lung resection, he teases the muscle and nerve away from the rib and then moves it out of the way before spreading the ribs. This reduces trauma to the muscle and intercostal nerve, dramatically reducing post-operative pain.

His study of 160 patients published in the June, 2008 issue of *The Annals of Thoracic Surgery*, a medical journal, showed that those who received the new technique reported reduced pain in the hospital and at 3, 4, 8 and 12 weeks after surgery. They required less pain medications and were more likely to return to normal activities eight to 12 weeks after surgery. The new technique is becoming increasingly popular. Surgeons from Denmark, the Netherlands, Germany, France and Spain recently traveled to UAB to observe Dr. Cerfolio perform the procedure and learn the technique.

## ASK THE EXPERT: IMPROVING TREATMENTS FOR CHILDREN WITH BONE CANCER

**OSTEOSARCOMA, the most common form of bone cancer, accounts for about 3 percent of all childhood cancers.** It often occurs in the bones around the knee or the arm bone near the shoulder. Like other cancers, osteosarcoma can spread beyond the bone into nearby tissue or travel through the bloodstream to other bones, or to the lungs and other organs.

Texas Children’s Hospital, an internationally recognized, full-care hospital located at the Texas Medical Center in Houston, is a leader in the treatment of osteosarcoma. It has done pioneering work in the molecular biology of pediatric bone tumors and clinical applications of genomics. Health and Wellness discussed this progress with Dr. Ching Lau, co-director of the cancer genomics program and hematology service and associate professor of medicine and oncology at the Baylor School of Medicine.

**Q: How are you using advances in molecular biology to improve treatments for osteosarcoma?**

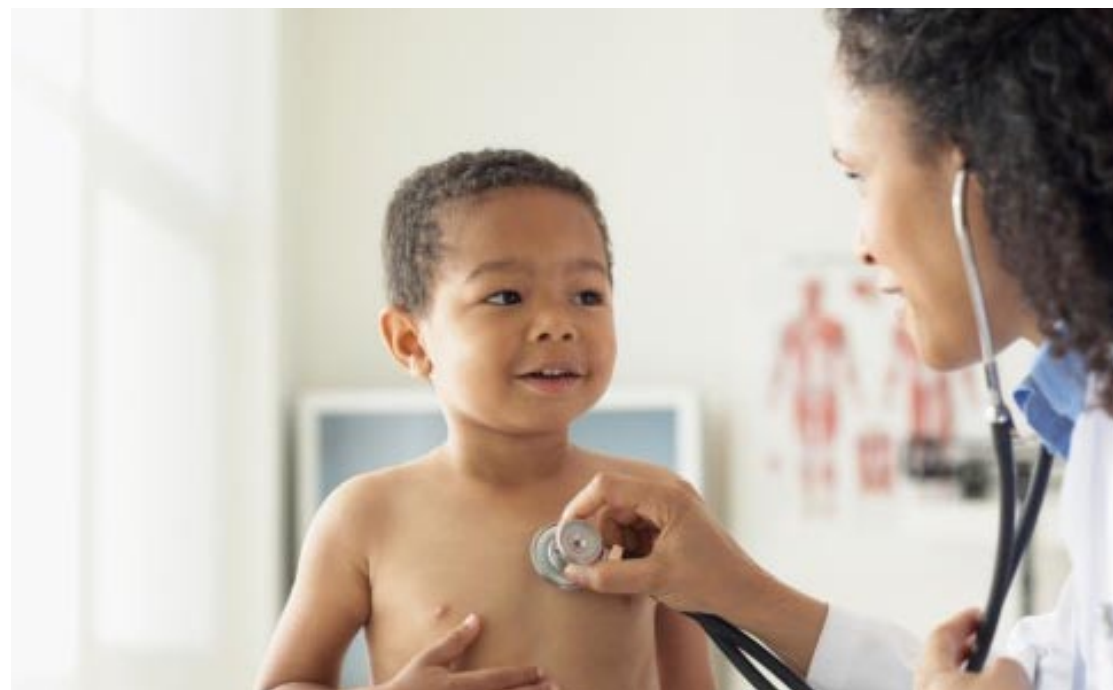
**A:** The most common treatment is a combination of chemotherapy and surgery. Treatments may begin with chemotherapy, followed by surgery and then more chemotherapy. However, some patients respond well to chemotherapy, while others don’t.

To improve results, we came up with a hypothesis that said that every cancer cell’s biological behavior is determined by its genetic makeup. If we can find the genetic changes that these cells undergo, then we can determine who will respond well. After lots of work, we came up with a molecular signature of 45 genes that helps predict who will respond well to chemotherapy in the pre-op period. Now we are taking this research to the next level of critical development, where we will be carrying out this study with 1,400 pediatric patients in the US and Europe. We hope this will be the defining study to make an accurate prediction of who will do well with chemotherapy, key information in preparing a treatment plan.

A second project is aimed at high-risk patients, children who have not done well after preoperative chemotherapy. Their prognosis is not good. Our project addresses the question of whether there is something we can do to suppress the genes that make the cancer cells resistant to chemotherapy and then manipulate the genes in such a way so that the cancer cells are converted into good responders to chemotherapy. We have come up with a way of doing this.

Data shows that the time it takes for the cancer cells to metastasize to the lungs is a sign of prognosis. If no metastases are detected in the lung before preoperative chemotherapy but metastases are evident after preoperative chemotherapy, the prognosis is poor. However, if we can figure out in advance who will develop these lung metastases and give them more aggressive chemotherapy treatment in the pre-op period, then they will do better later. To accomplish this, we have developed a second genetic signature that predicts at the time of diagnosis who will develop metastases to the lung even if they show no clinical signs.

We are very excited about these clinical trials because they enable us to personalize medicine and give each patient the precise therapy that will have the best results for his or her particular cancer. Although quite rare, osteosarcoma is a devastating disease. At one time, nearly all children with osteosarcoma had to undergo amputation of part of their legs or arms. Today surgeons are able to perform “limb sparing” surgery to remove the tumor without amputation. However, these surgeries can be disfiguring. Chemotherapy is also difficult for these children, so we want to improve its effectiveness so that treatment will be not only effective but easier on them.



Texas Children’s Hospital is a leader in the treatment of osteosarcoma, and has done pioneering work in the molecular biology of pediatric bone tumors.

RHP 11  
NYU CANCER INSTITUTE

## PATIENT'S REPORT: HELPING A LITTLE LEAGUER STAY IN THE GAME

**IN JANUARY, a 13-year-old Little Leaguer in San Francisco caught a bad break when he developed a germ cell tumor in the brain.** Although germ cell tumors are rare, making up only 4 percent of cancer in children and adolescents, they are serious because they can spread to the spinal cord and other parts of the body. Because metastatic germ cell tumors require more therapy and have poorer outcomes, predicting in advance of treatment which tumors are likely to spread is crucial. Managing these children's treatment is also difficult because the side effects of surgery, radiation and chemotherapy can have lasting effects.

Since only 2.4 children out of 1 million are diagnosed with germ cell tumors each year, few physicians have treated the condition. The Little Leaguer's parents recognized that their son required state-of-the-art diagnosis and treatment, so they took him to Children's Hospital and Research Center Oakland. The only independent children's hospital in Northern California, Children's Hospital and Research Center Oakland offers outstanding patient care and supports nationally recognized teaching and research. Founded in 1912, it has a specialized staff and facilities to treat rare illnesses and health problems like germ cell cancers.

"As the name implies, germ cell cancers got their name from the word germinate," says Dr. Joseph Torkildson, director of the neuro-oncology program at Children's Hospital and Research Center Oakland. "These cancers

### PREDICTING WHETHER GERM CELL TUMORS WILL SPREAD TO THE SPI- NAL CORD PAYS OFF IN SURVIVAL AND QUALITY OF LIFE.

usually occur in the ovaries and testes, but they can also be found in other parts of the body, such as the brain." The stage for germ cell cancers is set before birth. Most germ cells migrate to the reproductive organs when the embryo is developing. According to the American Cancer Society (ACS), about 10 percent of germ cells fail to make this journey and end up in the head, chest or upper back of the developing fetus. Later in life, tumors may develop in the areas of the reproductive organs and other parts of the body where the germ cells migrated.



*When it comes to rare cancers, such as germ cell tumors in children and adolescents, it's critical to choose a treatment facility that specializes in that specific disease.*

"Symptoms vary depending on the location of the tumor," says Dr. Torkildson. "Patients who have germ cell cancers in the pineal region of the brain report headaches and vomiting." Those like the Little Leaguer who have germ cell cancers in the suprasellar region near the pituitary gland develop hormonal abnormalities and symptoms like increased urination and thirst, common signs of diabetes. Diagnosing germ cell cancers and ruling out other conditions can therefore be tricky. Advanced imaging equipment such as that used by neuroradiologists at the Children's Hospital and Research Center in Oakland helps locate the tumor and determine the likelihood that the cancer will spread.

"Obtaining this information increases the chances of long-term survival because we can

come up with a more aggressive treatment plan," says Dr. Torkildson. "The quality of life of these patients is also enhanced because they will get the optimal doses of radiation and chemotherapy so that side effects will be less." Dr. Kenneth W. Martin, a pediatric radiologist who specializes in neuroimaging at the Children's Hospital and Research Center Oakland, came up with a technique to provide this data. "Two years ago, we began looking for nodules on nerves in the spines of these patients before they received treatment," says Dr. Martin. "Our hypothesis was that patients who had nodules were at higher risk for having the cancer spread and should receive more extensive radiation."

The theory proved to be correct and a major help in formulating a treatment plan for the Little Leaguer. Extra radiation was

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UAB HEALTH SYSTEM

applied to the boy's brain as well as the area in the spine where the nodules had shown up on the scan. The youth also completed extensive chemotherapy treatments. Follow-up tests revealed that his tumor was completely gone.

"In addition to our high-tech treatments, we emphasize the human side of patient care," says Dr. Martin. "We have an extensive child life program that helps children express their concerns and offers them techniques to manage anxiety during procedures." Treatment plans are designed to enable patients to live as normal a life as possible. The Little Leaguer's treatments were scheduled so that they would not conflict with his games. While undergoing chemotherapy and radiation treatments, he helped pitch his team to first place and was named to the league's all-star game.

The team at Children's Hospital and Research Center Oakland tapped the boy's fondness for sports by using sports metaphors to explain treatments. They also encouraged his friends and teammates to support him during tough times. When he lost his hair during chemotherapy treatments, 10 of his friends shaved their heads too. "But our work isn't done," says Dr. Martin. "We want other young patients with germ cell tumors to experience favorable results. I've been presenting our findings at professional meetings, so that other physicians will screen for nodules on nerves in the spinal cord too. This process only requires an extra five minutes, but it makes a tremendous difference for patients with germ cell tumors."

## SYMPTOMS OF HEAD AND NECK CANCERS OFTEN OVERLOOKED

### NEED ANOTHER REASON TO QUIT SMOKING?

**In addition to blackening our lungs and making it difficult to breathe, smoking also is a major risk factor for head and neck cancers.**

"About 50,000 Americans develop head and neck cancers each year," says Dr. Bert O'Malley, Jr., chair of the department of otorhinolaryngology—head and neck surgery, University of Pennsylvania School of Medicine in Philadelphia. "People who smoke should talk to their doctors about ways to quit because head and neck cancers can affect taste, speech and swallowing as well as appearance." In addition to smoking, alcohol use is also a major risk, according to the National Cancer Institute. Head and neck cancers are more common in men and individuals over 50.

The Center for Head and Neck Cancer at Penn provides comprehensive diagnostic evaluation and treatment. The multidisciplinary team includes experts in head and neck surgery, radiation oncology, medical oncology, oral and maxillofacial prosthetics, ophthalmology, pathology, radiology and a center for cranial bone surgery. Team members also include nurses, speech and swallowing therapists, nutritionists, rehabilitation therapists and social workers.

Head and neck cancers typically begin in the squamous cells in the moist tissues in the mouth, nose and throat. Common symp-

toms include a lump that does not heal and a sore throat that lingers. Some people have difficulty swallowing or experience hoarseness. Symptoms are often overlooked or attributed to other health conditions. In the past, physicians relied on physical examinations to evaluate the oral and nasal cavities, neck, throat and tongue. Ultrasound technology, which uses sound waves to construct a highly detailed image on a computer screen, is being used to examine the head and neck. "Ultrasound has made a major difference," says Dr. O'Malley. "It helps us evaluate lymph nodes in the neck after treatment and visualize neck and parotid masses that are difficult to see."

In 2006, surgeons at the center introduced another technological advance: "robotic hands" to make incisions, sutures, and other delicate surgical maneuvers more accurate. Called Transoral Robotic Surgery (TORS), this novel approach to treat benign as well as cancerous lesions was developed at the center. "TORS is a minimally invasive technique that allows us to overcome some of the difficulties of operating in the oral cavity, pharynx and larynx," says Dr. O'Malley. "Blood loss is reduced and patients experience less post-operative pain. They spend less time in the hospital and return to their normal activities more quickly."

The center also offers gamma-knife radiosurgery for both benign and malignant tumors of the head and neck. Despite its name, there is no blade or knife. Instead, the high-tech device delivers a dose of gamma radiation to the tumor with surgeon-like precision. "Patients usually require one treat-

### PEOPLE OVER 50 ARE MORE LIKELY TO DEVELOP THESE MALIGNANCIES.

ment and no general anesthesia with the gamma knife," says Dr. O'Malley, "which is a major advantage for patients who are not good candidates for conventional surgery."

Because it attracts so many patients, the center takes part in clinical trials. For example, one trial is investigating the use of a potent raf-kinase inhibitor in the treatment of metastatic thyroid cancer. "Our department is also doing research in the genetic basis for head and neck cancer," Dr. O'Malley says. "We expect these studies to result in new ways to treat head and neck cancers with vaccines, so patients will have more options."



*As if lung cancer weren't enough of a reason to kick the habit, smoking is also a major risk factor for head and neck cancers, which afflict some 50,000 Americans each year.*

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## VACCINE TAPS IMMUNE SYSTEM TO FIGHT OVARIAN CANCER

**ALTHOUGH THE INCIDENCE of ovarian cancer is low – about 2,500 women in the United States are diagnosed each year – the malignancy is difficult to treat and its diagnosis is challenging.** In its earliest stages, ovarian cancer produces few if any signs. When symptoms like abdominal pain, unexplained changes in bowel and bladder habits and persistent indigestion occur, many women attribute the signs to other conditions. Unlike breast and prostate cancers, for which there are screening tests such as mammography or PSA levels, no such tests exist to identify ovarian cancers when they are in their earliest stages and most treatable.

Consequently, in more than 70 percent of women with ovarian cancer, the malignancy has already spread beyond the ovaries by the time it is diagnosed, making treatment more difficult, according to the National Cancer Institute. “But what also is significant is that even if patients have a good response to surgery and chemotherapy, 80 percent relapse,” says Dr. Kunle Odunsi, attending surgeon in the department of gynecologic oncology and co-leader of the Tumor Immunology and Immunotherapy Program at Roswell Park Cancer Institute in Buffalo, New York, the nation’s first cancer research, treatment and education center (founded in 1892) and the only National Cancer Institute–designated comprehensive cancer center in upstate New York. “This makes finding more effective therapies a top priority.”

To overcome the problem, Dr. Odunsi and colleagues are collaborating on a promising vaccine that unleashes the power of the immune system to destroy ovarian cancer cells that remain after surgery and chemotherapy treatments. “Our vaccine boosts the body’s ability to seek out and kill ovarian cancer cells that display a ‘foreign’ protein, NY-ESO-1,” he says. “This foreign protein [antigen] is not found on non-cancer cells, but some ovarian cells do not display it either.” The team’s therapeutic vaccine trains the immune system to recognize the small changes that signal that a cell may be cancerous.

Early studies of the vaccine’s effectiveness have been encouraging. The team tested the experimental anti-tumor vaccine in 18 women who had completed surgery to remove their ovarian cancers and who were receiving chemotherapy to destroy any remaining cancer cells. The vaccine did not cure the cancer, but it did get the immune system to make anti-



*A promising vaccine that trains a patient’s own immune system to target ovarian cancer cells offers hope in the treatment of this notoriously difficult malignancy.*

bodies and specialized cells with the capacity to kill ovarian cancer targets. The vaccine also appeared to lengthen the time until tumors reappeared. “The medical progression-free survival was 19 months,” says Dr. Odunsi. “This was significant because some women had relapsed as many as eight times,

### EARLY STUDIES SHOW PROMISE IN PATIENTS WITH ADVANCED DISEASE WHO HAVE RELAPSED

and had been free of tumors for only a couple of months.”

Further research is underway to improve the vaccine’s effectiveness. The team is exploring ways to keep cancer cells from hiding from the immune system and heightening the immune system’s ability to respond to the vaccine. Dr. Odunsi’s colleague, Dr. Adam Karpf of the department of pharmacology and therapeutics at Roswell Park, is looking for new ways to encourage all the ovarian cancer cells to display the NY-ESO-1 antigen,

so that the immune system will destroy them. His research is the first step in determining whether a combination of the anti-tumor vaccine, a drug called decitabine, and chemotherapy drugs now used in treatment will be effective in patients with advanced cancers.

To accomplish his goal, Dr. Karpf will use decitabine, a drug that is currently used to treat other disorders in which cell growth is out of control. Decitabine changes the DNA, turning the genes that code for the ovarian cancer antigen, NY-ESO-1. Once the cells are producing the antigen, Dr. Karpf will treat them with chemotherapy drugs to make certain that the chemotherapy is still effective against the ovarian cancer cells, even though the DNA has been altered. Dr. Karpf’s research may include numerous changes in the order the drugs are given and the time between doses.

“Coming up with a vaccine is a very long and involved process,” says Dr. Odunsi. “We at Roswell are fortunate to be working with other organizations like the Cancer Vaccine Collaborative Program and the Ludwig Institute for Cancer Research on critical research.” ■

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