

Ahead of the Curve

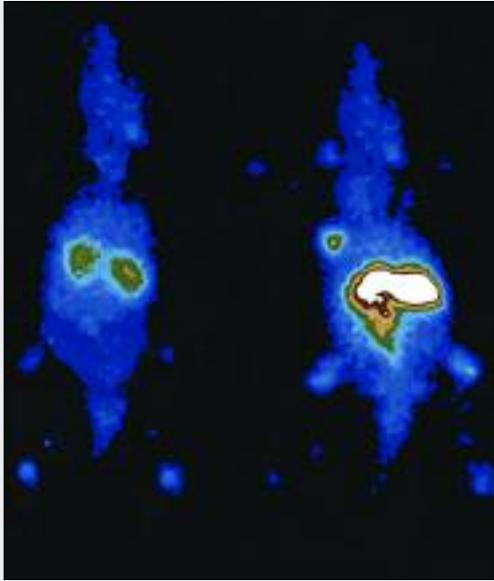
Head and Neck Cancer
Forging new paths



**YALE-NEW HAVEN
HOSPITAL**

Head and Neck Cancer

A new arsenal of weapons in the war on cancer



“Speech makes us unique as humans, and our faces are the signature of our individuality. Head and neck cancer attacks both.”

—Clarence Sasaki, MD

A full 30 years have passed since the nation declared war on cancer and called for a commitment comparable to the effort to land a man on the moon. Scientists were confident they would have the disease beat by the end of the century, but here we are, in 2005, with a new report announcing cancer has eclipsed heart disease as the number one killer of American men and women under age 85.

The good news is that deaths from both diseases are falling. Cancer deaths have declined about one percent a year since 1999 thanks to earlier detection, more effective prevention efforts and better treatments. The battle against some types of cancers has fared better than others. Lung cancer in men and colon cancer, in particular, have declined as smoking rates decline and screening increases. Deaths from head and neck cancer remain fairly constant, however.

About 40,000 Americans each year are diagnosed with head and neck cancer—a cluster of cancers that attack the nose, sinuses, ears, throat, larynx, thyroid, salivary glands and the lymph nodes in the neck. These cancers represent about three percent of the total number of cancer cases in the U.S. The overwhelming majority, about 95 percent, of malignant tumors in the head and neck region are squamous cell cancers. Squamous cells line many of the structures in the head and neck such as the mouth, nose and throat. The remaining 5 percent are cancers of the salivary glands. Surgery, radiation and chemotherapy continue to be the standard treatments.

“Although the number of people who develop these cancers is not huge, these diseases are often devastating,” said Clarence Sasaki, MD, chief of otolaryngology at Yale-New Haven Hospital (YNHH) and the Charles W. Ohse Professor of Surgery at the Yale University School of Medicine. “Speech makes us unique as humans, and our faces are the signature of our individuality. Head and neck cancer attacks both. And the effects of treatment can be traumatic. Patients may feel weak and nauseated from radiation and chemotherapy, and surgery can be both disfiguring and leave patients without the ability to speak or swallow.”

The good news is that significant improvements in surgery, reconstructive techniques and rehabilitation have already immeasurably improved the quality of life of patients with head and neck cancers, but the most exciting possibilities are now just beginning to take shape in the laboratory.

Along the way in the war against cancer, scientists have learned a lot about how cancer works at the molecular level, from its first awakening in the aberrant DNA of a single cell’s nucleus to its assault on the body. Armed with that information, researchers have been developing a broad array of weapons to attack the disease at every step along the way. Many of these therapies are in clinical trials, and scientists are hopeful they may someday revolutionize cancer treatment.



← Dermatologic and Laser Surgery



Targeting EGFR

A promising area of research focuses on EGFR, a receptor for a protein called epidermal growth factor (EGF), which blankets two-thirds of all head and neck cancers. Cetuximab (Erbix®), a monoclonal antibody targeted against the EGFR, has been designed through laboratory processes to bind to the EGFR. This binding action is believed to prevent or reduce the replication of the cancer cells.

A recent trial conducted by researchers affiliated with the Erbix Head and Neck Study Group included 417 patients with locally advanced head and neck cancer. Approximately half of the patients were treated with cetuximab plus high-dose radiation therapy; the other half was treated with high-dose radiation therapy only. The average duration of survival was 58 months in the group of patients treated with cetuximab/radiation, compared with only 28 months for those treated with radiation only. The only notable side effect associated with cetuximab was a skin rash.

The researchers concluded that cetuximab and high-dose radiation significantly improve survival compared to high-dose radiation therapy alone in the treatment of locally advanced head and neck cancer. The drug appears to provide comparable survival benefits to chemotherapy in the treatment of these patients, without the associated side effects.

On the horizon

Unlike chemotherapy and radiation, which destroy cancer cells and healthy cells alike, these new medicines home in on cancer cells and target their weakest links. Among the new cancer fighters are the antiangiogenesis drugs, which keep tumors from growing their own blood supplies. Tumors, like any other cells, need oxygen and nutrients to survive. They first invade healthy tissue, looking for blood vessels to tap for these essentials. Eventually, they start to grow their own capillaries and vessels. Angiogenesis inhibitors prevent tumors from building those pipelines.

More than 50 angiogenesis inhibitors are being studied in humans. Thus far, only a tiny number of human patients treated with these compounds have seen their tumors shrink or disappear. Clinicians are nonetheless encouraged; while angiogenesis inhibitors don't make cancer go away, they appear to slow tumor growth. Some of these therapies prevent chemical growth factors from reaching tumors, blocking signals that would otherwise instruct the cell to grow out of control. Others drive cancerous cells to self-destruct. Still others block enzymes that cancer cells need to take over healthy tissues to give themselves room to grow.

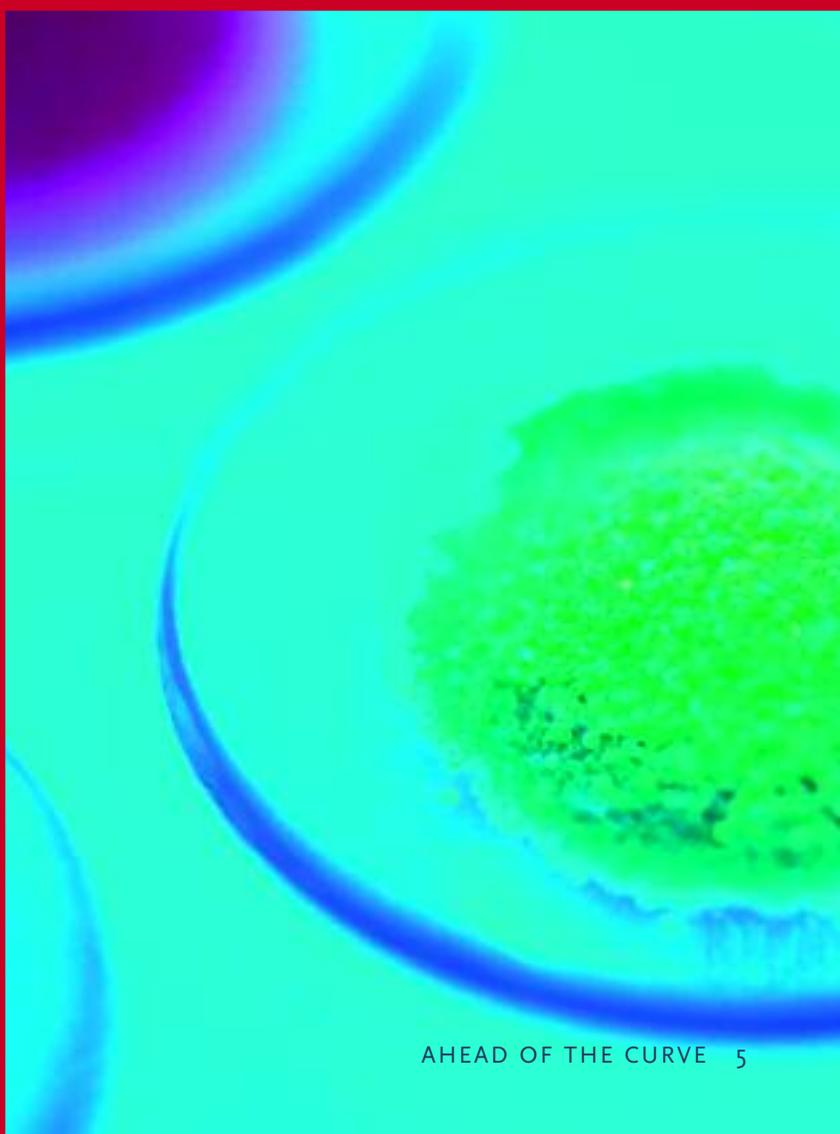
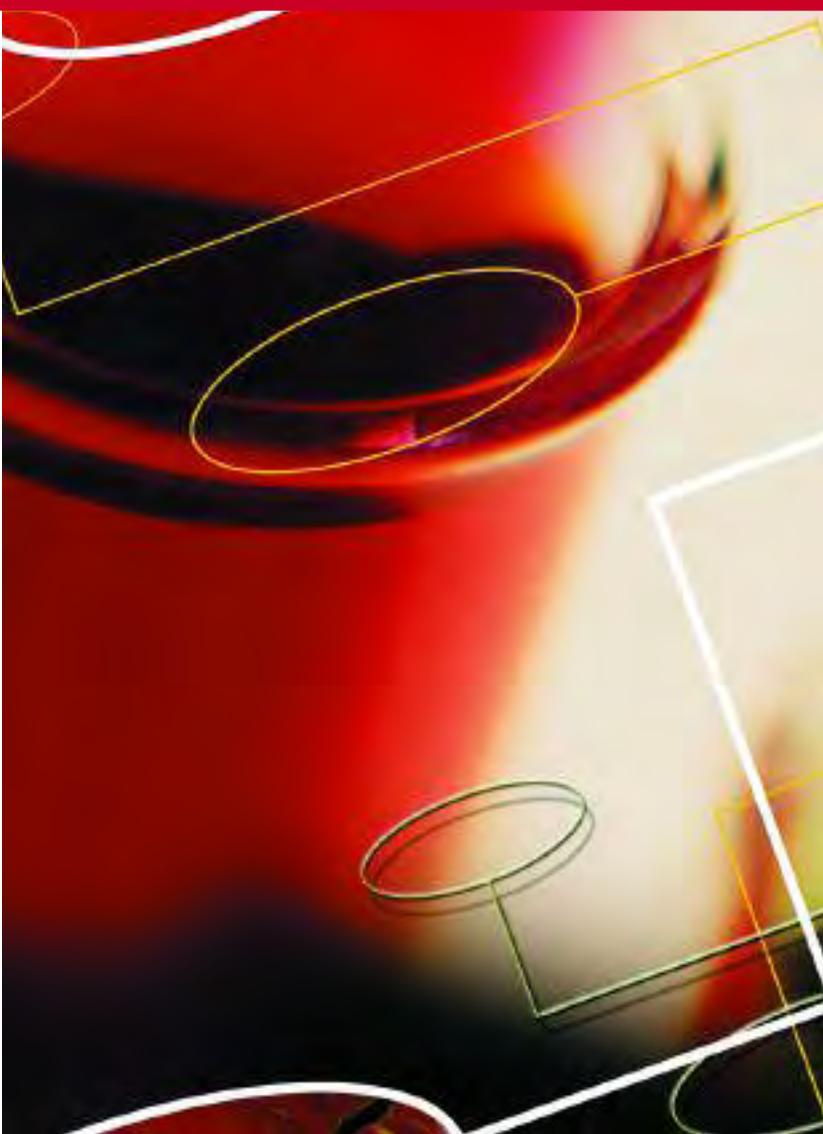
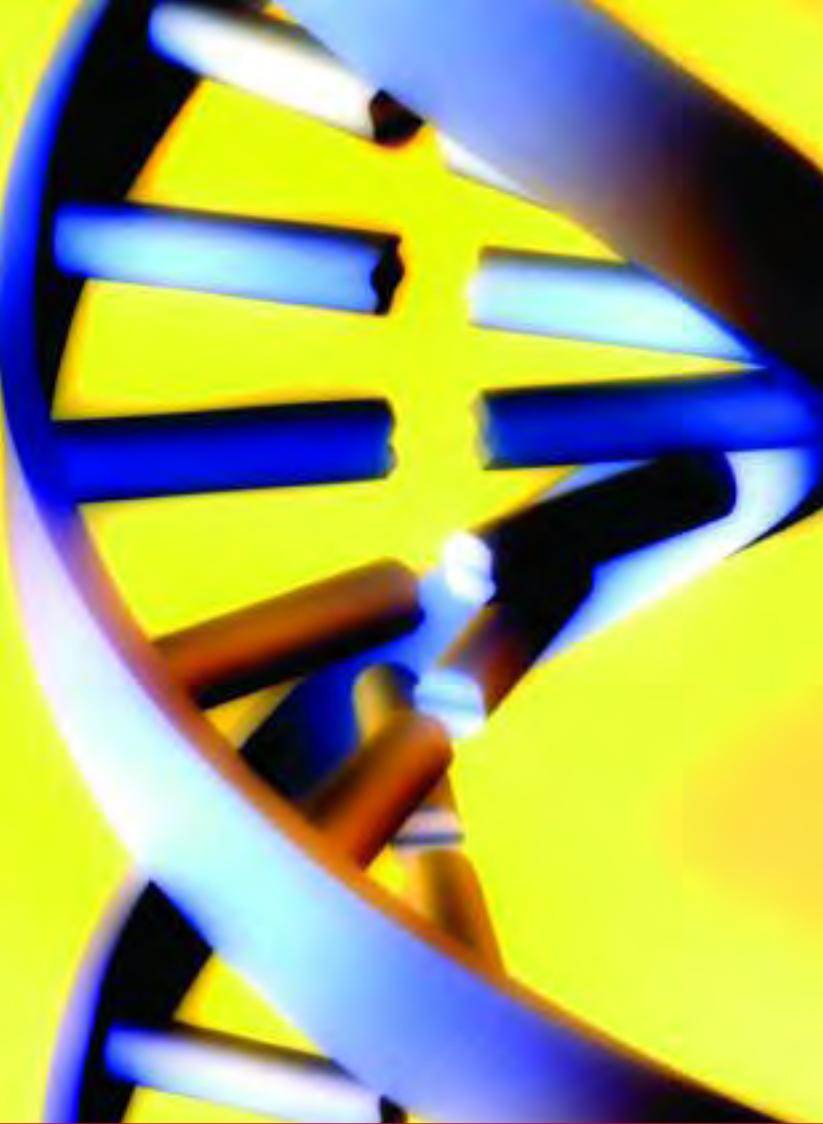
Some experts believe that by tinkering with the cancer cell's biology, new therapies may transform cancer from a life-threatening illness to a chronic but manageable one similar to diabetes and high blood pressure. For example, researchers at IDEC Pharmaceuticals developed the first drug to successfully target proteins on cancer cells. Scientists learned that cancer cells are studded with an unusually large number of receptors. These receptors provide a site that growth factors and other compounds essential to the survival of a cancer cell can plug into in order to fuel the cells' growth. The drug, Rituxan, is the first monoclonal antibody approved in the U.S. for the treatment of cancer. It is a molecule specifically engineered to fit into the receptors on non-Hodgkin's lymphoma cells and, in this case, single out the cancer cell for destruction by the immune system. Herceptin, a drug that keeps growth factors from feeding certain kinds of breast-cancer cells, is another potential success story.

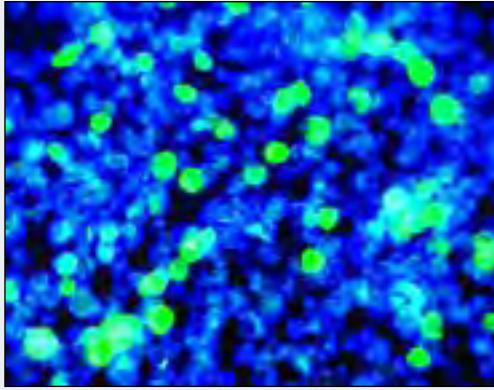
Scientists have been focusing on a receptor called EGFR, which is host to a protein called epidermal growth factor (EGF). Two-thirds of all cancer types, including head and neck cancers, are blanketed with EGF receptors. Scientists believe that growth-factor inhibitors may weaken a tumor enough for chemotherapy to finish it off.

Who's at risk?

Whether you're talking about conventional therapy or one of these promising new approaches, experts agree the earlier you catch a cancer, the better your chances of controlling it.

"Head and neck cancer is predominantly a cancer of our middle and senior years although we are seeing younger patients," said Dr. Sasaki. "We have patients in their mid-20s and 30s with cancer of the





One of the real dangers of this cancer is that in its early stages, it can go unnoticed. It can be painless, and little in the way of physical changes may be obvious.

tonsil, which we didn't see two decades ago. We're also seeing more cases of cancer of the throat among women."

Risk factors include:

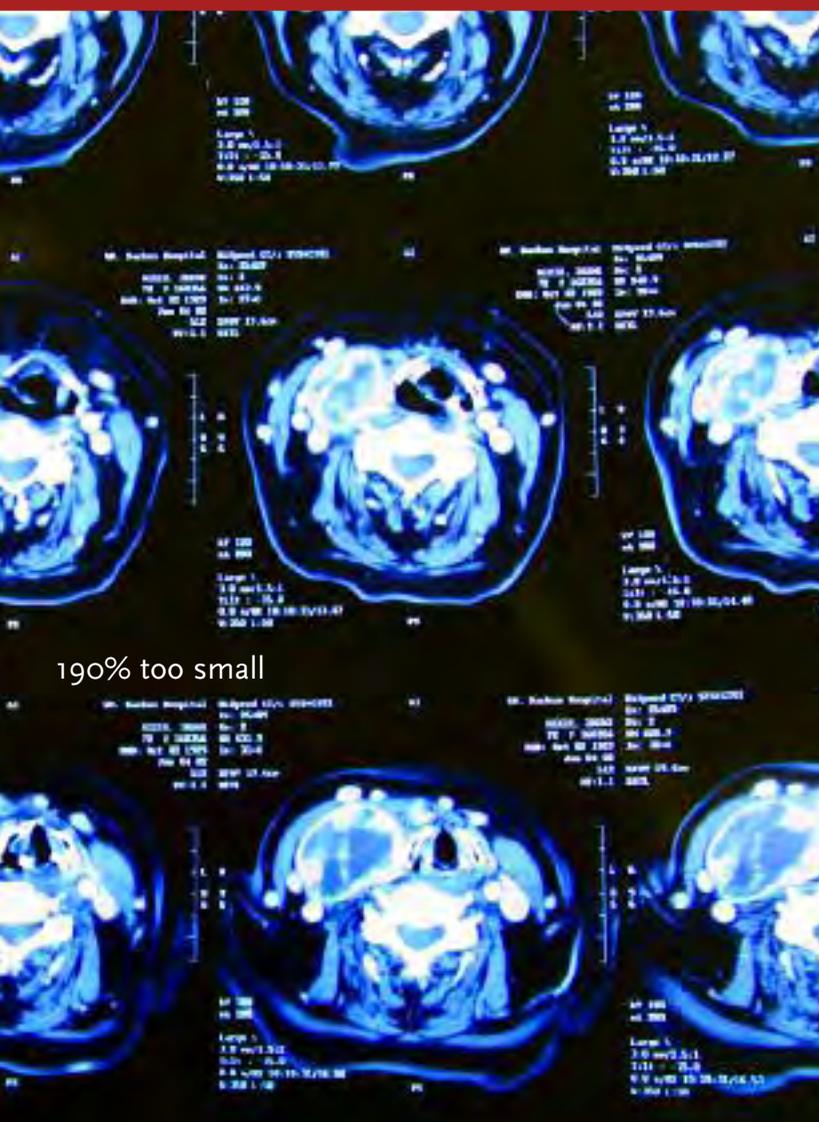
- ▶ Tobacco use—tobacco use in all its forms is number one on the list of risk factors. At least 75 percent of those diagnosed with head and neck cancers are tobacco users. When tobacco is combined with heavy alcohol use, the risk is significantly increased, as the two act synergistically. Those who both smoke and drink have a 15 times greater risk of developing oral cancers.
- ▶ These cancers usually develop when patients are in their 50s, 60s and 70s, after decades of tobacco use. Head and neck cancer does occur in those under this age, however. These may be young men who use chewing tobacco or others who may develop a cancer with a viral-based causal link.
- ▶ For decades this cancer affected men six times more often than women, but that ratio is changing, and some estimates now place the incidence at 2:1.
- ▶ Ultraviolet radiation has been identified as a risk factor for cancers of the lip as well as other skin cancers.
- ▶ Radiation exposure is implicated in several head and neck cancers.
- ▶ Biological factors include viruses such as some strains of the human papilloma virus (HPV), a sexually transmitted virus that infects about 40 million Americans.
- ▶ Certain industrial exposures such as wood or nickel dust and asbestos have been implicated in some head and neck cancers.
- ▶ There are studies that indicate a diet low in fruits and vegetables could be a risk factor, and that conversely, one high in these foods may have a protective value against many types of cancer.

Diagnosis: the earlier the better

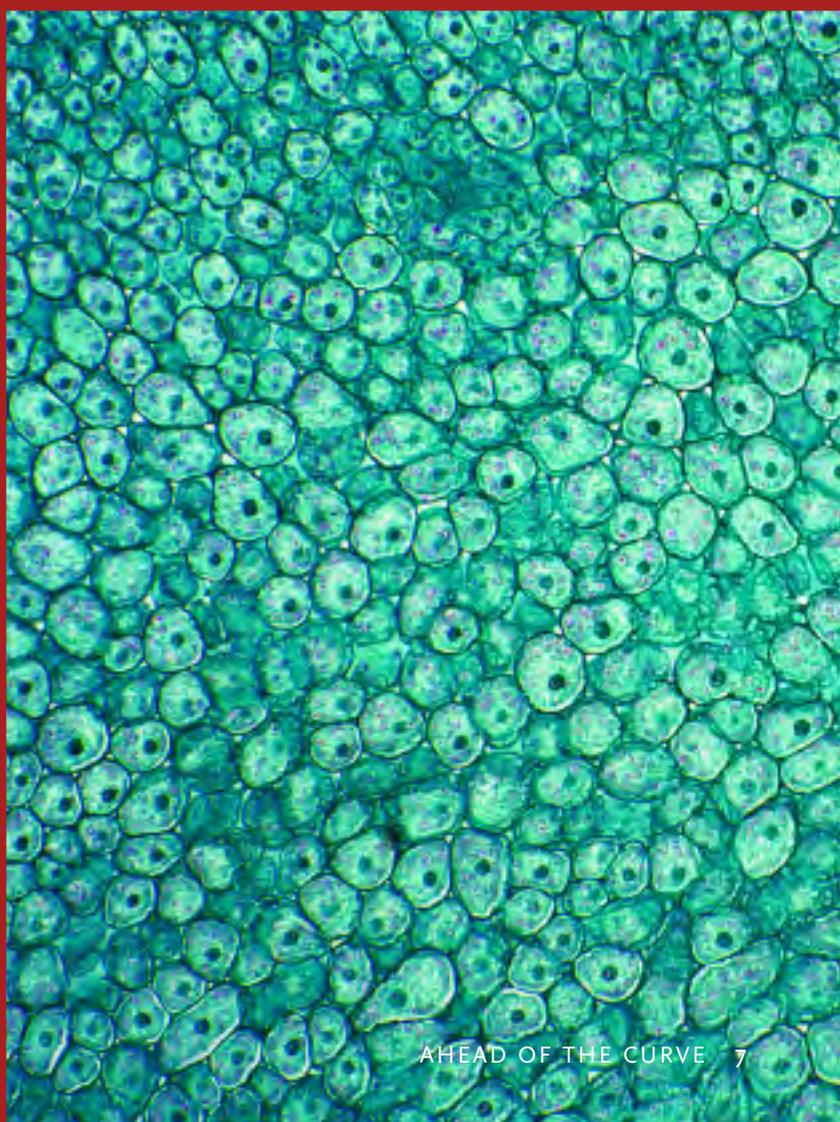
One of the real dangers of this cancer is that in its early stages, it can go unnoticed. It can be painless, and little in the way of physical changes may be obvious. When people do go to their doctors they may complain of a lump in their neck, a sore on the tongue, difficulty or pain with swallowing, hoarseness, ear pain or bleeding from a sore in the mouth. How far advanced the cancer is often depends on its site. Patients with cancer of the vocal cords may come in early, when the cancer is confined to the larynx because it causes hoarseness when it is still small. Other tumors such as those in the supraglottic larynx or the hypopharynx often are quite large before they cause noticeable symptoms.

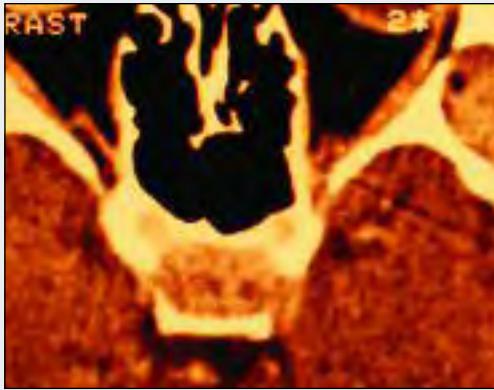
Signs and symptoms

"Our dream is to have an effective screening tool such as the PSA test for prostate cancer," said John Joe, MD, assistant professor of



190% too small





The most common symptoms of head and neck cancer include:

- ▶ Any sore in the mouth or throat that does not heal within three weeks
- ▶ Neck or jaw pain that radiates to the ear
- ▶ Abnormal growth in the mouth
- ▶ Lump in the neck that remains for more than three weeks
- ▶ Chronic cough or hoarseness
- ▶ Sore throat that does not improve
- ▶ Difficulty swallowing food or liquids
- ▶ Coughing up blood

otolaryngology. Unfortunately, there are currently no effective screening tests for head and neck cancers although scientists are searching for biochemical or molecular markers that might alert them to the presence of these cancers. Advances in technology have made it possible to screen blood samples for protein patterns specific to head and neck cancer. Researchers have developed a classification system using these protein patterns that was able to successfully distinguish between cancer patients and healthy smokers with an accuracy of 80 to 92 percent.

Diagnosis and finding the best care for head and neck cancer

Head and neck cancer is diagnosed by a combination of a medical history, physical examination, various imaging studies (CAT scans, MRI scans, PET scans) and biopsies of the tumor. A biopsy is the only sure way to confirm whether a suspected lesion is cancer. A surgeon removes tissue and submits it to a pathologist who examines it under a microscope to check for abnormal or malignant cells.

Another new way to test for oral cancer before a biopsy is beginning to be used by dental professionals. A dentist uses a small brush to gather cell samples of a suspicious area. The specimen is then sent to a lab for computer analysis. In a recent study of 945 patients, this system, called Oral CDx, detected all cases of oral cancer correctly, even when dentists didn't suspect the presence of cancer from a lesion.

Making treatment decisions

One of the most difficult issues following a cancer diagnosis is choosing where to get treated. Head and neck cancers are life-threatening, complex diseases that can best be treated by a team of specialists in an advanced practice setting. Where you first receive care is critically important since the course of the disease is defined by its initial treatment.

"You only get that first chance to cure a cancer once," said Dr. Yung H. Son, MD, director of Head and Neck Radiation Oncology and professor in the Department of Therapeutic Radiology at Yale-New Haven Hospital. "If that first effort fails, the chances of curing a recurrence is significantly lower." Receiving the right treatment from the start can significantly increase a patient's chance for a cure. A study in the *Journal of the American Medical Association* showed that mortality rates were 40 to 80 percent lower for cancer patients in hospitals that had the most experience performing particular surgical procedures. In-depth experience in treating specific kinds of cancers can have a dramatic effect on a patient's chances for a cure.

You will want to choose a medical center known for constantly pushing the boundaries of what can be done through medical research and advanced practice in head and neck cancer. Specialists at advanced practice hospitals employ the latest proven treatment methods, use state-of-the-art technology and adopt new patient care programs to treat the whole patient.





Caring for the whole patient

Surgery, radiation, chemotherapy as well as novel investigational treatments are critical parts of the success story in the war against cancer, but caring for the concerns, fears and anxieties of patients and their families are at the heart of the best treatment plans.

“At the beginning of our relationship with patients, we focus on providing information and answering questions and concerns. By the time they have been treated and are recovering, we know their personal histories, the names of their grandchildren, what scared them the most and what worked best for them,” said Shelley Jolie, RN, BSN, the ear, nose and throat nurse coordinator. “Their willingness to share their experience helps us be more effective in supporting the next patient.”

Once a month, head and neck cancer patients have an opportunity to meet and talk with one another, with Jolie and with social worker Mary Crooks, an essential part of the head and neck cancer care team.

Yale-New Haven Hospital has been recognized as being one of the top 25 hospitals for the treatment of cancer by *U.S. News & World Report*, and the Yale Cancer Center is one of a select network of 38 comprehensive cancer centers in the nation designated by the National Cancer Institute. What does this mean? A Comprehensive Cancer Center must perform research in three major areas: basic research; clinical research; and cancer prevention, control and population-based research. In addition, it must conduct activities in outreach and education, directed toward both healthcare professionals and healthcare consumers.

There are so many factors to consider before launching your personal fight against cancer, from finances to the emotional strain on loved ones. Yale-New Haven Hospital’s team of head and neck cancer specialists has the expertise and resources to provide everything you might need to take care of your cancer: diagnosis, treatment, reconstruction, psychosocial support for you and your family, pain management, rehabilitation and assistance in returning to your life after cancer. Dr. Sasaki leads a multidisciplinary group of healthcare professionals—head and neck surgeons, radiation oncologists, chemotherapy oncologists, physical and speech therapists, plastic surgeons, advanced practice nurses and social workers as well as a patient advocate. This team approach gives newly diagnosed patients a carefully determined treatment plan focused on providing the most comprehensive, effective care possible. The actual curative treatments are usually surgery and radiation with chemotherapy added to decrease the possibility of the cancer spreading to other parts of the body and for those patients whose cancer has already metastasized.

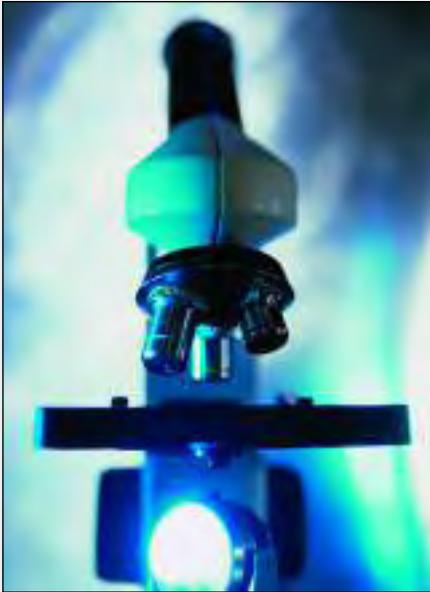
Less invasive surgeries; reconstructive breakthroughs

In the last decade surgeons have learned new surgical procedures that permit removal of tumors from complex areas that were not possible in the past while also preserving organ function and facial appearance to a far greater degree than was possible just a few years ago—all while keeping cure of the cancer as the main goal. “Our primary goal is still eliminating the cancer, of course, but also we’re focusing on the quality of life by preserving swallowing and speaking functions and minimizing disfigurement,” said Dr. Sasaki. “Many of the advances that have been introduced or developed here at Yale contribute to patient comfort and lifestyle.”

The radical neck dissections that were the standard of care until the 1980s have been replaced in many cases by less radical surgeries that preserve nerves, arteries and muscles in the neck. Patients continue to move, speak, breathe and eat normally after surgery. Patients with throat cancer who a few years ago would have lost their vocal cords and their

Dr. Clarence Sasaki, upper left and right, is a master of surgical techniques that preserve organ function and appearance. Toni Taylor, LPN (lower right) monitors the vital signs of Art Trickey of Cheshire during one of the weekly head and neck cancer clinics. Dr. Steve Leder helps patients relearn how to swallow after surgery.





Staging: what is it?

Before treatment can begin, cancer specialists use a variety of techniques to determine the extent of the disease, to see if the cancer has spread, and if so, where. This process is called “staging.” Staging is very important because it gives important diagnostic information in addition to defining therapy. Once the stage of the cancer is known, an individualized treatment plan can be developed. It is important to understand that while staging is critical to determine the best treatment plan, each individual and each cancer are unique. While statistics indicate individuals who are diagnosed with advanced cancers have poorer outcomes, it doesn’t necessarily mean that any one individual with advanced cancer will have a bad outcome.

Each type of cancer is staged according to specific characteristics. The most widely used system in the United States for staging cancer is called the TNM System. It describes the extent of the primary tumor (T stage), the absence or presence of spread to nearby lymph nodes (N stage) and the absence or presence of distant spread, or metastasis (M stage).

(Continued on page 14)

voices can often be treated with a supraglottic laryngectomy, a less invasive surgery that preserves critical structures. Patients who undergo this surgery maintain their ability to speak although they need to learn new ways to swallow. At YNHH rehabilitative specialists led by Steven Leder, PhD, work with patients to help them adjust to and overcome some of these impairments.

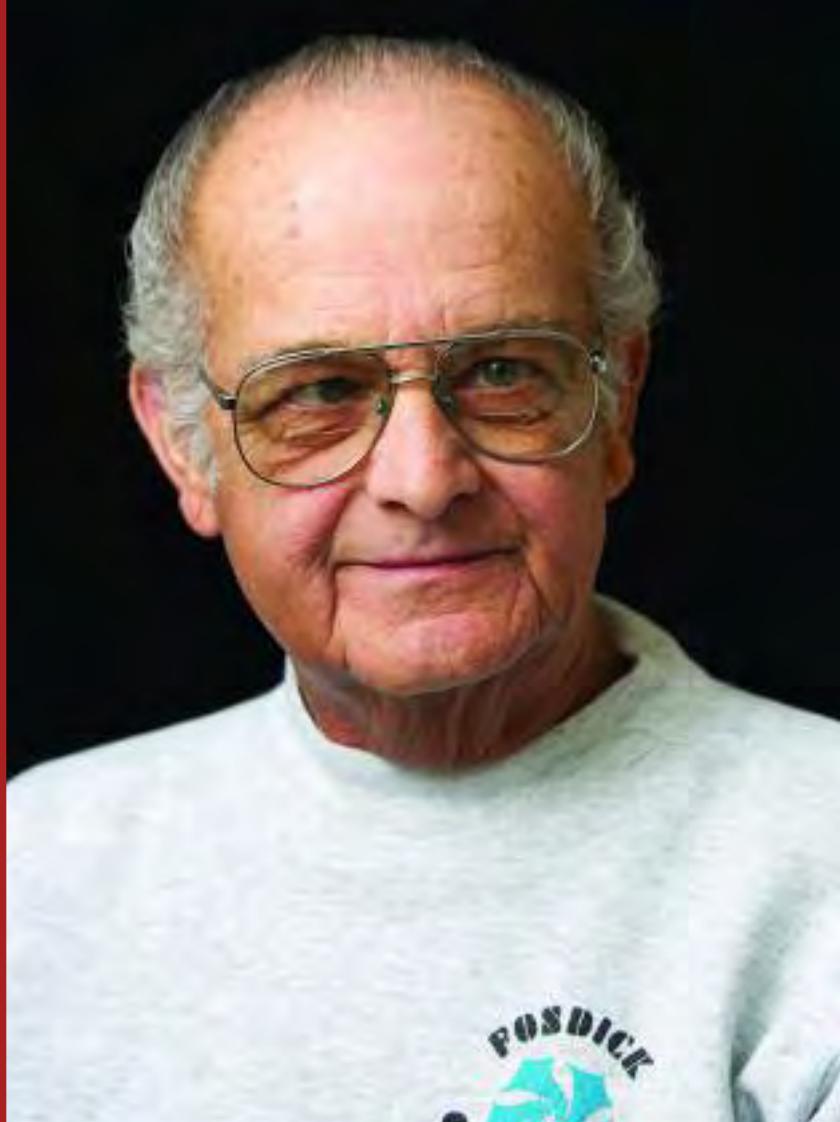
One of several pioneering approaches to head and neck cancer developed at YNHH, sentinel node radiolocalization is a minimally invasive technique that makes it possible to examine a patient’s lymph nodes—the part of the neck where cancer is most likely to spread—to determine what type of neck surgery, if any, is needed.

One of the most exciting new surgical advances is the use of laser surgery to remove certain throat cancers using an endoscopic probe in the mouth. This technique allows surgeons to remove tumors without an open incision in the neck. “This surgical technique was developed in Germany about a decade ago,” said Dr. Sasaki. “Initially American head and neck surgeons, myself included, were skeptical about its effectiveness, but I have been performing it for almost two years now, and I’m a believer. It is just as effective in removing the cancer as more invasive surgeries and patients heal more quickly. They get out of the hospital sooner, are able to swallow earlier and have fewer postoperative infections. The downside is that it can be used only in very specific areas in the larynx.”

Breakthroughs in reconstructive surgery represent one of the biggest success stories for head and neck cancer patients. Reconstructive surgery has improved dramatically, yielding previously unattainable cosmetic and functional outcomes. Research data indicate that the results of complicated surgical procedures like these reconstructions are best accomplished by specialists such as the team at YNHH who perform them on a regular basis.

Some of these techniques were pioneered at Yale-New Haven where a team of microvascular, oral, plastic and otolaryngology surgeons, led by Douglas Ross, MD, works together to repair areas of the head and neck that have been removed or impaired as a result of surgery to remove the cancer. In some cases, patients lose their tongues, palates, teeth, cheeks and even entire sections of their jaw. Skin, muscle, bone and tiny microscopic veins and arteries supporting them are removed and reattached at the site of the deficit. Tissue from the forearm, abdomen or shin is often used, and “sometimes we can reinnervate the nerves in the skin, too, which helps patients learn how to swallow again,” said Dr. Ross.

Current and former patients alike are welcomed to attend the monthly Head and Neck Cancer Support Group. Recent attendees include, clockwise: Barbara Ryan, New Haven; Raymond Rutledge, Jr., Meriden; Deborah Zergibel, Hamden, and Wilfred Fountain, Meriden.



The TNM System involves using the letters T, N and M to assess tumors by:

- ▶ The size of the primary tumor (T)
- ▶ The degree to which regional lymph nodes (N) are involved and
- ▶ The absence or presence of distant metastases (M)

Once the T, N and M are determined, a stage of I, II, III or IV is assigned:

- ▶ Stage I—the cancer is less than 2 centimeters in size and has not spread to the lymph nodes in the area.
- ▶ Stage II—the cancer is between 2 and 4 centimeters and has not spread into the lymph nodes.
- ▶ Stage III—The cancer is either more than 4 centimeters or the cancer may be smaller but it has spread to nearby lymph nodes.
- ▶ Stage IV— The cancer has spread to other parts of the body.

The genetic makeup of cancer is being increasingly recognized as an important prognostic factor. For example, some genes have been associated with an aggressive course or tendency to recur. Identification of these genes in an early-stage cancer may indicate a poor prognosis. Some research suggests that the genetic makeup of the cancer may be even more important for determining prognosis than the stage of the cancer.

Radiation: wielding new age weapons

“The goal of radiation therapy is to sneak in the biggest dose of radiation in the shortest amount of time as possible,” said Dr. Yung H. Son. “We want to direct the radiation precisely at the tumor and minimize damage to any surrounding healthy tissue.” This balancing act forms the basis of modern radiation therapy.

There is a whole arsenal dedicated to radiation therapy—external beam radiotherapy machines such as linear accelerators and betatrons, which produce x-rays and gamma rays of increasingly greater energy. Intensity modulated radiation therapy, also known as IMRT, when used alone or combined with surgery, has been shown to greatly increase the chance for survival for patients with head and neck cancer. IMRT delivers high doses of radiation directly to cancer cells in a very targeted way, much more precisely than is possible with conventional radiotherapy. IMRT can be used to treat tumors that might have been considered untreatable in the past due to the close proximity of vital organs and structures. This has important advantages in oral cancers as it allow the beams to hit their target area while missing the surrounding structures such as the salivary glands.

One new approach that is being evaluated is intraoperative irradiation in which a large dose of external radiation is directed at the tumor and surrounding tissue during surgery. Scientists are also investigating drugs called radiosensitizers to increase the chances of tumor cells being damaged and radioprotectors to protect normal tissue.

Dr. Son was one of the first radiation oncologists in the U.S. to use a combination of brachytherapy, which involves implanting tumors with tiny metallic seeds containing radioactive isotopes, with external radiation therapy to cure head and neck cancers that could not be removed surgically.

Radiation therapy is often given in conjunction with surgical treatment, but studies are showing that in some cases, radiation therapy—sometimes combined with chemotherapy—is just as effective as surgery. These new approaches can often preserve the ability to speak and swallow normally, even in patients with advanced disease.

Chemotherapy update

Surgery and radiation are very effective weapons in treating head and neck cancer in localized areas, but once cancer has spread to other locations, chemotherapy has an important role in treatment. When these three treatments are used together, their complementary avenues of attacking the disease frequently offer the patient the best chance to beat cancer. Many different kinds of drugs are used as chemotherapy agents; the choice of which drug to use depends on the specific type of head and neck cancer being treated.

A grateful patient created a tribute in fabric to the team of head and neck specialists who treated her.





IMRT benefits

Intensity modulated radiation therapy, (IMRT) has been shown to greatly increase the chance for survival for patients with head and neck cancer, according to a 2004 study published in the *International Journal of Radiation Oncology-Biology-Physics*. Beginning in 1997, 74 patients with squamous cell carcinoma of the oropharynx were treated with IMRT. Seventy percent of the patients were at Stage IV, a very advanced stage of cancer. After treatment, the estimated four-year survival of all patients was 87 percent. Eighty-one percent of those patients were estimated to be completely disease free after completing treatment. Those patients who had surgery in addition to being treated with IMRT improved their chances survival dramatically to 92 percent. Without surgery, 66 percent of the patients survived.

Another important finding of this report is that the use of IMRT also reduced painful side effects of the treatment and allowed for more normal post-treatment salivary function.

A number of recent clinical trials have studied the effectiveness of administering chemotherapy concurrently with radiation. In one recent national study of nasopharyngeal cancer, a rare form of head and neck cancer in the U.S., radiation therapy alone was compared with concurrent chemotherapy and radiation. Patients who received chemotherapy with radiation had a decreased risk of distant metastases. They experienced both prolonged disease-free survival and prolonged overall survival. Three-year results showed a 46 percent survival rate in the radiation therapy group vs a 76 percent survival in the chemotherapy/radiation group. Thus, the integration of chemotherapy with radiation has changed our standard of care in nasopharyngeal cancer.

Because head and neck cancers vary widely in their response to chemotherapy, researchers are looking at biological markers that might be used to determine whether a particular cancer will be sensitive to a particular chemical agent. One such experimental tool, the histoculture drug response assay, might one day permit rapid testing of cancer cells' response to commonly used chemotherapeutic drugs before treatment.

Asking the right questions

A diagnosis of cancer can make you feel out of control and overwhelmed. Learning about the disease and asking questions can help patients regain a sense of control. Very few cancers require emergency treatment, so take the time to learn about your disease; ask questions and seek a second opinion before agreeing to any treatment plan.

Questions to ask your doctor

- ▶ Do you treat many patients with my diagnosis?
- ▶ What stage is my cancer?
- ▶ Is there anything in particular about my cancer that makes my prognosis better or worse?
- ▶ What are my treatment options?
- ▶ Is the goal of my treatment to cure my cancer or stop it from growing?
- ▶ When will we know if the treatment is working?
- ▶ What are the risks and side effects associated with each treatment?
- ▶ Will I be able to continue to work during my treatment?
- ▶ Am I an appropriate candidate for a clinical trial?
- ▶ What happens after I complete treatment?
- ▶ What happens if my cancer comes back?

An experienced, multidisciplinary team of healthcare professionals ensure YNHH head and neck cancer patients receive the most advanced care. Social worker Mary Crooks, MSW (upper left) plays an essential role in supporting the psychosocial needs of patients. Lynn Acton, speech therapist, (upper right) teaches patients to speak again after surgery. Dietician Crystal Reil, RD, (lower left) counsels a patient on food choices. Shelley Jolie, RN, and Toni Taylor, LPN, review a patient's chart.





Publications

The following is a small sampling of recent publications written by Yale's head and neck cancer group. Call 203-785-2593 for a complete updated list.

- ▶ Yu, Z., Weinberger, P., Haffty, B., Sasaki, C., Rimm, D.L. & Psyrri, A., "β-Catenin Functions Mainly as an Adhesion Molecule in Patients with Squamous Cell Cancer of the Head and Neck," *Clinical Cancer Research* (In Press).
- ▶ Weinberger, P., Yu, Z., Kowalski, D., Joe, J., Psyrri, A. & Sasaki, C., "Differential Expression of EGFR, c-Met and c-Erb-B2 in Chordoma Compared to 18 other Malignancies," *Arch. Otol. Head and Neck Surg.* (submitted).
- ▶ Yu, Z., Weinberger, P., Haffty, B., Sasaki, C., Zerillo, C., Joe, J., Kowalski, D., Dziura, J., Camp, R.L., Rimm, D.L. & Psyrri, A., "Cyclin D1 is a Valuable Prognostic Marker in Oropharyngeal Squamous Cell Carcinoma," *Clinical Cancer Research*, Vol. 11, No 3, 2005, pp 1160-1166.
- ▶ Weinberger, P., Yu, Z., Haffty, B., Harigopal, M., Kowalski, D., Sasaki, C., Rimm, D.L. & Psyrri A., "Prognostic Significance of p16 Protein Levels in Oropharyngeal Squamous Cell Cancer," *Clinical Cancer Research*, Vol. 10, No.17, 2004, 5684-91.
- ▶ Ross, D.A., Hundal, J.S., Son, Y.H., Ariyan, S., Shin, J., Lowlicht, R.A. & Sasaki, C.T., "Microsurgical Free Flap Reconstruction Outcome in Head and Neck Cancer Patients After Surgical Extirpation and Intraoperative Brachytherapy," *Laryngoscope*, 114:1170-77, 2004.

Where to learn more

As part of your research, you may want to browse the Internet. The Web has a staggering amount of information to help you understand your disease, make crucial treatment decisions and cope with the burdens of illness, but sorting through all the information can be overwhelming. Type "cancer" into a search engine like Google and you will get more than 85 million results. Narrow it down to head and neck cancer, and you still have more than 374,000 pages to wade through. Here are some sites designed to help patients learn more:

- ▶ Yale-New Haven head and neck cancer specialists:
www.yaleheadandneck.org
- ▶ National Cancer Institute resource for head and neck cancer:
<http://www.cancer.gov/cancertopics/types/head-and-neck/>
- ▶ Support for People with Head and Neck Cancer Internet resource listing: <http://www.spohnc.org/resources.html#Resources>
http://patient.cancerconsultants.com/head_cancer_news.aspx
- ▶ American Cancer Society:
<http://www.cancer.org/docroot/home/index.asp>
- ▶ National Coalition for Cancer Research:
<http://www.cancercoalition.org/>

Clinical trials

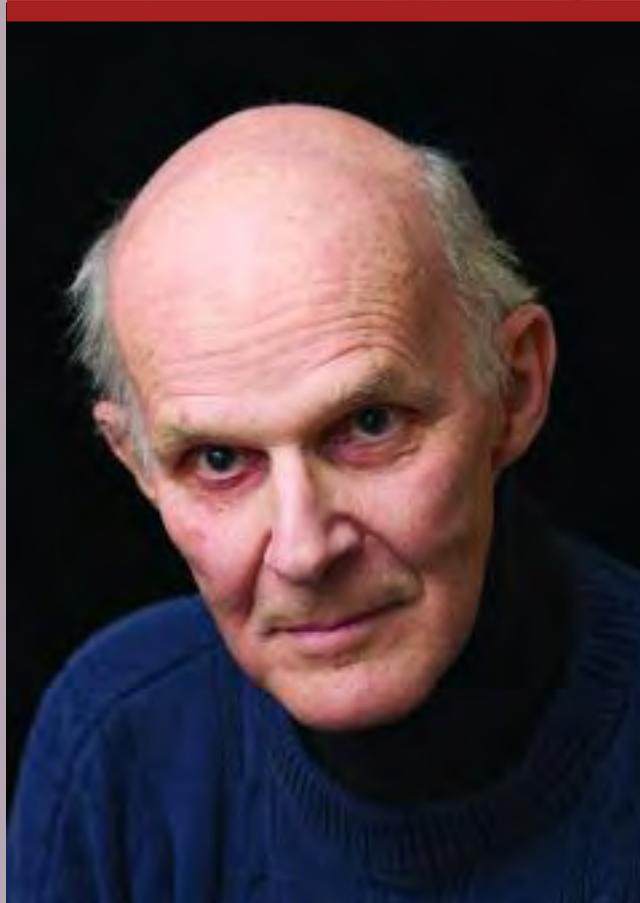
To find out what clinical trials are currently recruiting patients, call 203-785-2593.

- ▶ Phase I/II Trial Capecitabine (XEL) and Mitomycin-C (MC) used concurrently with accelerated concomitant boost radiation therapy (CB-RT) in head and neck cancer (SCCHN)
- ▶ Phase III study comparing Iressa to Methotrexate in recurrent metastatic head and neck cancer
- ▶ ECOG Protocol E2303, entitled, "Phase II Evaluation of C225 Combined with Induction Paclitaxel and Carboplatin Followed by C225, Paclitaxel, Carboplatin and Radiation for Stage III/IV Operable Squamous Cancer of the Head and Neck" and the ancillary science to this study, entitled "Correlation of EGFR Expression and EGFR Related Signaling Pathway to Antitumor Response to Therapy with C225 and Induction Chemotherapy and Chemoradiation in Patients with Operable Stage III/IV Head and Neck Squamous Cancer"
- ▶ Cetuximab plus docetaxel + oxaliplatin in platinum refractory patients

Dr. Ziwei Yu (right) studies the expression of different biomarkers in head and neck cancer using automated in situ quantitative analysis. Dr. Yu reported his findings in a recent paper published in Clinical Cancer Research that demonstrated the importance of a biomarker, called nuclear cyclin D1, in determining the best treatment for patients with oropharyngeal squamous cell cancer.



Ahead of the Curve



Support group participants include, top, left to right: Arlene Daigle, Middletown, CT; Eleanor Pawelczyk, Kensington, CT; bottom, left to right: Karl Crawford, New Haven, CT and Patricia Mead, St. Petersburg, FL.



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