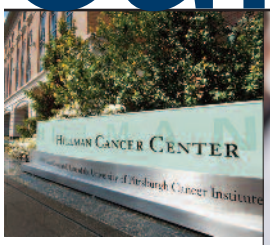
UPMC Cancer Centers

cancerinsights



Hillman Cancer Center is the academic hub of the UPMC Cancer Centers network. The state-of-the-art facility offers cutting-edge cancer care and also is home to the research activities of the University of Pittsburgh Cancer Institute (UPCI). UPCI is the only center in western Pennsylvania with the elite Comprehensive Cancer Center designation from the National Cancer Institute.

To learn more about clinical research or patient care opportunities at UPCI and UPMC Cancer Centers, please call **412-647-2811** or visit our website at **www.UPMCCancerCenters.com.**

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medical oncology

Clinical trials of ABT-888 PARP inhibitor showing promise in treatment of many cancers

The University of Pittsburgh Cancer Institute (UPCI) is a hotbed for some very cool science in the earliest stages of drug development for the treatment of cancer. Through its Molecular Therapeutics/Drug Discovery Program, UPCI is using its scientific foundation to support the development of small-molecule anticancer agents and novel therapeutic approaches for the treatment of cancer.

Among the drugs showing the highest potential is the category of poly ADP ribose polymerase (PARP) inhibitors, which have been shown to improve chemotherapy's effectiveness by lowering the resistance of cancer cells to treatment. The PARP family of enzymes is involved in a number of cellular processes, including DNA repair and programmed cell death.

The PARP research program at UPCI was started under the leadership of the late Merrill J. Egorin, MD, professor of medicine and pharmacology and chemical biology at the University of Pittsburgh School of Medicine. Dr. Egorin, who recently lost his own battle with cancer, was the coleader of the UPCI Molecular Therapeutics/Drug Discovery Program and codirector of the UPCI Clinical Pharmacology Analytical Facility. He, like many other researchers, was intrigued by the possibilities that ABT-888 and other PARP inhibitors presented.

continued on page 3 >>>

Celebrating the Past, Shaping the Future

The recent economic downturn of the past few years has affected every aspect of our society, and none of us has been immune to the market slump.

Yet, as physicians and scientists, we can't allow the rise and fall of the Dow to deter us in our mission to defeat cancer — especially now that we have made such tremendous progress in treating cancer, increasing detection, and decreasing morbidity and mortality rates. If anything, the cyclic nature of the economy contrasts with the constant and unrelenting nature of this disease, and illustrates how constant and unrelenting we must be in our fight against it.

The University of Pittsburgh Cancer Institute (UPCI) and UPMC Cancer Centers remain steadfast in our commitment to this fight. Toward that end, we recently completed our pentennial National Cancer Institute review, which is required to maintain our status as an NCI-designated Comprehensive Care Center. This prestigious designation denotes that our cancer center has wide-ranging laboratory, clinical, and population-based research, combined with transdisciplinary research that bridges all of these scientific areas. It also demonstrates our commitment to professional and public education and to translating our clinical and research advances into the communities we serve.

The completion of our most recent NCI review dovetails nicely with our commemoration of UPCI's 25th Anniversary. As we celebrate this significant milestone in our institution's history, we also celebrate the milestones that have been achieved in cancer research and care over the past quarter century. Along that path, our understanding of cancer has advanced thousandfold, and more people are alive today because of our increased knowledge of this disease.

The foundation of UPCI has always been to accelerate the translation of what we're learning in our labs to the clinical application of that science at the bedside. Our physician-researchers are on the frontlines of translating scientific discovery into the everyday practice of medicine. This edition of *Cancer Insights* focuses on some of those discoveries. Among them are scientific breakthroughs with exciting potential for understanding the virology of cancer; utilizing the latest techniques in radiation oncology technology; and developing molecular diagnostics that may change the surgical response to certain cancers.

Also highlighted are a number of promising clinical trials using PARP inhibitors, being conducted by some of the brightest physician-researchers in the field. We are in the enviable position of not only cultivating the newest crop of scientific discoveries, but also the newest crop of scientists.

I hope you will be as fascinated by these breakthroughs as we are proud to report them to you. I look forward to continuing our partnership as we work toward a future without cancer.

Sincerely,

Nancy E. Davidson, MD

Director, University of Pittsburgh Cancer Institute and UPMC Cancer Centers

Associate Vice Chancellor for Cancer Research and Hillman Professor of Oncology

Professor of Medicine,
University of Pittsburgh School of Medicine

medical oncology

>>> continued from front page

Recognized by his peers for his dedication to improving cancer treatments and supporting the next generation of researchers, Dr. Egorin was awarded a Translational Research Professorship by the American Society of Clinical Oncology in 2009. He was using funding from the award to continue his preclinical and clinical studies of the PARP family of enzymes and how they work as cancer therapies. One role being explored is the use of PARP inhibitors with cytotoxic chemotherapy.

According to Nancy E. Davidson, MD, director of UPCI and UPMC Cancer Centers, Dr. Egorin was equally passionate about research, as well as mentoring young researchers.

"He was also concerned with caring for patients with cancer, even long before he was diagnosed," says Dr. Davidson. "His commitment to cancer patients, his laboratory, his students, and the cancer institute will be greatly missed, but his legacy will endure."

Dr. Egorin oversaw a group of some of the best and brightest physician-researchers in the country, several of whom have embarked on separate National Cancer Institute (NCI)-sponsored Phase I and Phase II clinical trials of ABT-888. It is through this group of physician-researchers that his research will continue.

Targeted therapy for difficult cancers

Kristin Zorn, MD, a gynecologic oncologist with the Magee-Womens Gynecologic Cancer Program of UPMC Cancer Centers, is the principal investigator for a Phase II trial that randomizes women between pegylated liposomal doxorubicin and ABT-888 with temozolomide for the treatment of ovarian, fallopian tube, and peritoneal cancers. The study is open to patients with recurrent disease, which is important because ovarian cancer is the second most common and most lethal gynecologic cancer and has few symptoms, which makes diagnosis difficult until the disease has started to spread.

Another study is looking at the combination of ABT-888 with carboplatin and paclitaxel in advanced solid malignancies, including ovarian, epithelial, pancreatic, peritoneal cavity, prostate, fallopian tube, and breast cancers, which show mutations of the BRCA genes. Leonard Appleman, MD, PhD, whose practice focuses on renal, prostate, and other genitourinary cancers, is the principal investigator for this study of adult patients who have already received at least two prior chemotherapy regimens.

Shannon Puhalla, MD, assistant professor at the University of Pittsburgh School of Medicine and breast oncologist at Magee-Womens Cancer Program of UPMC Cancer Centers, is the principal investigator of a monotherapy study of ABT-888. This trial will, for the first time, examine ABT-888 as a single agent for patients with cancers related to the genetic mutation or dysfunction in the BRCA 1 or BRCA 2 genes, which predispose women to breast and ovarian cancers.

"Cancer cells have been shown to have increased levels of PARP, which we believe causes resistance to chemotherapies and other cancer treatments," Dr. Puhalla explains. "Tumor cells in patients with BRCA mutations are particularly reliant on the mechanism of DNA repair that is inhibited by the PARP."

The PARP protein is important for repairing single-strand DNA breaks. If single-strand breaks are not repaired, they get converted to double-strand DNA breaks. People with the BRCA-mutated gene have tumors with a defect in repairing double-strand breaks, which, if not repaired, are lethal to the tumor cells.

In previous trials in which ABT-888 was used as a combination treatment, it appeared to inhibit PARP, making cancer cells more sensitive to the chemotherapy. "Our hope with this trial is that patients with BRCA mutations or certain other breast or ovarian cancers may respond to ABT-888 as a single agent, and avoid the toxicities of cytotoxic chemotherapies," Dr. Puhalla says.

"Our hope with this trial is that patients with BRCA mutations or certain other breast or ovarian cancers may respond to ABT-888 as a single agent, and avoid the toxicities of cytotoxic chemotherapies."
Shannon Puhalla, MD

Dr. Egorin shown with Drs. Puhalla and Tawbi.

The concept of PARP inhibition

Hussein A. Tawbi, MD, MSc, assistant professor of medicine, University of Pittsburgh School of Medicine, has been studying PARP inhibition since 2003. "The concept of PARP inhibition leading to cell death came as a surprise to the scientific community because it was thought that you had to damage DNA first with chemo then give a DNA repair inhibitor," he explains. "It turns out there are some cells inherently deficient in DNA repair, and if you give them a PARP inhibitor even without the chemo, you get 'synthetic lethality' and they die. Those cells were the BRCA-deficient cells. The synthetic lethality concept has proven effective in breast and ovarian cancer patients who were BRCA deficient."

Dr. Tawbi is currently the principal investigator on a Phase I study combining ABT-888 with carboplatin and paclitaxel in patients with advanced malignancies and liver or kidney dysfunction. He also is studying the combination of ABT-888 with modulators of other DNA repair pathways in melanoma cells. According to Dr. Tawbi, the BRCA 2 gene mutation is associated with a higher incidence of melanoma, but the monotherapy route does not appear to be effective on its own with melanoma patients. "To treat melanoma, we have to give a DNA-damaging agent first because you can't count on the BRCA gene to do it alone," he says.

For more information about these or any clinical trials currently being conducted by UPCI and UPMC Cancer Centers, please call 412-647-2811 or visit our website at www.UPMCCancerCenters.com.

UPCI researchers developing novel head and neck cancer therapies

Researchers from UPCI were recently awarded a patent from the U.S. Patent and Trademark Office for the development of a novel DNA therapy for head and neck cancers.

The therapy, developed by Jennifer R. Grandis, MD, professor of Otolaryngology and Pharmacology and Chemical Biology at the University of Pittsburgh School of Medicine and director of the Head and Neck Program at UPCI, and colleagues, Yukai He, MD, PhD, and Leaf Huang, PhD, University of Pittsburgh, targets the epidermal growth factor receptor (EGFR), a protein found on the surface of many types of cancer cells that cause them to multiply.

The newly patented treatment is based on a form of genetic therapy called "antisense" or AS, in which a synthetic strand of DNA or RNA targets the EGFR genes within a head and neck tumor. The AS drug is injected directly into the tumor, and works to block the production of a protein produced by the gene.

In the Phase I trial to determine the safety and potential toxicity of the drug as a single agent, the AS drug was not only well-tolerated, but caused tumors to shrink or disappear in 29 percent of patients studied, exceeding expectations. "Results from the Phase I study published in 2009 were surprisingly positive and show that EGFR AS therapy has great potential as a safe, effective treatment for head and neck cancers," says Dr. Grandis.

Based on the encouraging observations from the Phase I study, Dr. Grandis will participate in a Phase II trial with Athanassios Argiris, MD, professor of medicine and otolaryngology at the University of Pittsburgh, who will serve as principal investigator. The trial is being funded by a National Cancer Institute (NCI) R21 grant awarded to Dr. Argiris, which supports the development of innovative cancer clinical trials.

The Phase II clinical trial will incorporate the novel EGFR AS injections with the IV drug cetuximab and radiation for locally advanced head and neck cancer. "Our goal is to develop an efficacious and well-tolerated regimen that will be suitable for patients who cannot receive cisplatin, the drug most often used to treat head and neck cancers," says Dr. Argiris. "Cetuximab is an EGFR inhibitor that we're

able to use with patients who are not good candidates for chemotherapy because of age or other health problems, such as renal or kidney failure. We hope that the antitumor effects of cetuximab can be further boosted by the EGFR AS injections."

In addition to the clinical results, the researchers will be looking at a number of biomarkers in the tumor tissue, specifically the EGFR pathway, and how it can be affected with the two inhibitors — the cetuximab and the EGFR AS. They plan to do a baseline biopsy and another biopsy following treatment to evaluate biomarkers in the tumor.

The Phase II clinical trial will enroll patients who have advanced head and neck tumors that have spread to the lymph nodes in the neck that can be injected using ultrasound-guided injection, if necessary, as well as those with easily accessible mouth tumors. Selected patients must be poor candidates for chemotherapy either because of age (70+) or another health condition, such as renal or kidney failure. Patients will be evaluated by a team of radiation oncologists, medical oncologists, and head and neck surgeons to determine eligibility for the study.

For more information about enrolling a patient in the clinical trial, or the license for the patent, please call 412-647-2811 or visit our website at www.UPMCCancerCenters.com.

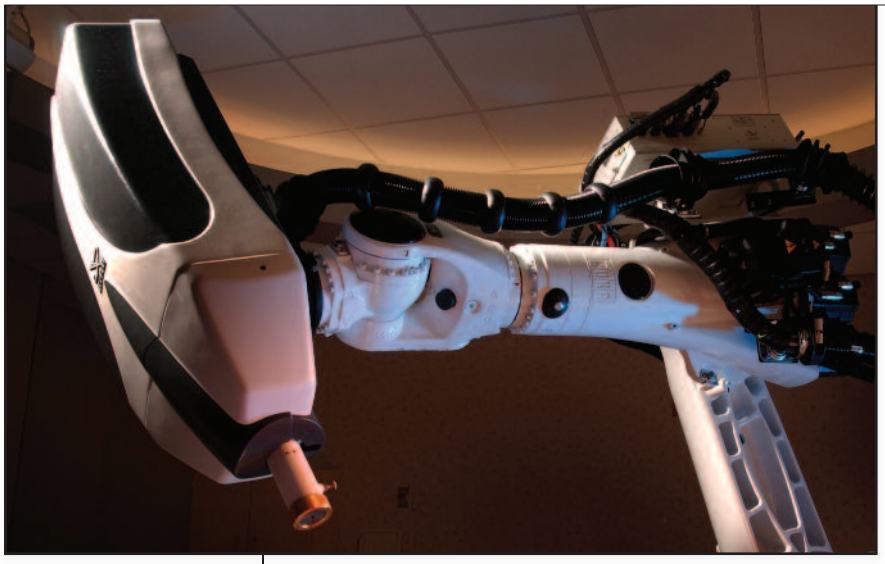
"We hope that the antitumor effects of cetuximab can be further boosted by the EGFR AS injections."

Athanassios Argiris, MD

Bevacizumab shown to improve results in recurrent metastatic breast cancer

Patients being treated for a certain type of advanced breast cancer for the second time may get better results if bevacizumab is added to their therapy, according to a multi-institutional study, of which UPCI was a major site, presented at the San Antonio Breast Cancer Symposium in December 2009. The study, which included 684 patients at 211 sites in 19 countries, evaluated the addition of bevacizumab to standard chemotherapy, showed an improvement in progression-free survival of women with metastatic breast cancer. Unlike chemotherapy, which kills cancer cells or keeps them from dividing, bevacizumab works to stop the growth of the cancer by blocking the formation of new blood vessels to inhibit blood flow to the tumor. Two prior clinical studies have shown the benefit of adding bevacizumab to chemotherapy as an initial treatment for advanced breast cancer. This trial was designed to see if the treatment would be safe and effective as a second treatment option.

radiation oncology



Stereotactic radiosurgery with Cyberknife shows promising results for pain control

Despite advances in cancer therapies, few options exist that effectively manage the pain associated with previously irradiated cancer that has spread to the bone or spine. As a result of a study completed at the University of Pittsburgh Cancer Institute (UPCI), however, patients with this type of pain may have a new option for treatment.

The study, led by Dwight E. Heron, MD, FACRO, director of Radiation Oncology Services, UPMC Cancer Centers, evaluated the use of stereotactic radiosurgery (SRS), a radiation therapy procedure pioneered at UPCI that precisely delivers a large dose of radiation to tumors, using CyberKnife®.

The two-arm study reviewed the outcomes of 228 patients treated with SRS at UPCI and Georgetown University Medical Center (GUMC). Most patients treated at UPCI received a single treatment with a mean of 16.3 Gy, while patients at GUMC generally received a mean dose of 20.6 Gy over three fractions.

Results from the study were presented last November at the annual American Society for Radiation Oncology conference in Chicago. The primary endpoint for the study was to evaluate the use of SRS to control pain associated with bone metastases. Both arms demonstrated that SRS is a safe and effective form of treatment for patients with cancer that has metastasized to the bone, even in patients who had previously received radiation to the spine. Pain control was significantly better in the single-treatment group for all measured time points up to one year after treatment (100 percent vs. 88 percent p=0.003). Local tumor control was significantly better in the group that received multiple treatments at time points up to two years after treatment (96 percent vs. 70 percent p=0.001). Similarly, the need for retreatment was significantly lower in the group that received multiple treatments (1 percent vs. 13 percent p<0.001).

"For patients with cancer that has metastasized to the bone or spine, conventional radiation therapy remains a very effective choice in alleviating cancer-related pain," says Dr. Heron. "However, for some patients with recurrent pain in sites that have previously been treated, few treatment options remain that can effectively manage pain without adversely affecting their quality of life. We are encouraged by the results of the study and are currently investigating these findings in a prospective clinical trial."

If you have a patient who may be a candidate for this type of treatment and would like more information about this study, contact Dr. Heron at herond2@upmc.edu.

"We are encouraged by the results of the study and are currently investigating these findings in a prospective clinical trial."

Dwight E. Heron, MD, FACRO

RapidArc embraced as an evolution in advanced delivery systems

As one of the nation's leading radiation oncology programs, the Department of Radiation Oncology at UPMC Cancer Centers has helped to define the use of many complex radiation treatment modalities, including such technologies as Gamma Knife® radiosurgery, which was pioneered by UPMC neurosurgeons and radiation oncologists in 1987, and the use of intensity-modulated radiation therapy (IMRT) to treat breast cancers and brain tumors, among others.

Considering the department's tradition and history of working with these complex treatment delivery systems,

it is not surprising that UPMC Cancer Centers would enthusiastically embrace and evaluate the next in a series of new technologies: RapidArc®.

According to Dwight E. Heron, MD, FACRO, director of Radiation Oncology Services, UPMC Cancer Centers, RapidArc is a natural evolution in advanced radiation therapy techniques.

"In many ways RapidArc is like IMRT. It uses all the advanced technologies that we have for target localization, immobilization, and imaging to harness the power of the radiation beam to destroy tumors, which are often in very tight, confined spaces that may not be accessible with conventional surgical approaches," explains Dr. Heron. "What is unique about RapidArc is that it takes the same type of complex, highly precise tailored treatment, and delivers the entire dose in two to three minutes compared to 20 to 30 minutes with IMRT."

An IMRT treatment plan often requires the delivery of radiation beams from multiple angles around the patient, requiring the patient to lie still on the table for lengthy periods of time to allow the radiation therapist to make repeated stops and starts to set up treatment. This setup increases the potential for inaccurate dose delivery if the patient and the tumor move during treatment. One of the main advantages of RapidArc technology, compared to conventional IMRT, is that it shortens the treatment delivery time, making it both more efficient and more accurate.

"With IMRT, we immobilize patients the best we can, but if they move during treatment there is a chance that some of the tissue that we intended to protect may get radiation, and some of the areas that we want to get treated won't," says Saiful Huq, PhD, FAAPM, FInstP, director of Medical Physics, Department of Radiation Oncology, UPMC Cancer Centers. "With RapidArc, you deliver the dose quickly; the patient doesn't have enough time to move, thus expediting treatment delivery, but also increasing patient safety."

RapidArc has the ability to rotate 360 degrees around the patient, and also gives physicists and radiation oncologists the ability to define the arc and to tailor the intensity of the beam from multiple angles throughout treatment to decrease radiation exposure to healthy surrounding tissue.

Since introducing RapidArc, UPMC Cancer Centers has used this new technology to treat head and neck cancers, brain tumors, lung cancers, gynecologic cancers, and rectal cancers with much success.

"We hope to use our experience pioneering other radiation oncology modalities, like IMRT, to expand the greater radiation oncology community's understanding of this important technology to treat other cancers as well," says Dr. Heron.

For more information about UPMC Cancer Centers' RapidArc program, please contact Dr. Heron at herond2@upmc.edu or Dr. Huq at huqs@upmc.edu.

UPMC Cancer Centers named top treatment site for Cyberknife

UPMC Cancer Centers' Mary Hillman Jennings Radiation Oncology Center recently was recognized as the top treatment site for overall use of the CyberKnife® at UPMC Shadyside — both in the United States and in the world — at the 2010 CyberKnife Society Scientific Meeting, held in March in Dallas. The CyberKnife Society is a non-profit organization dedicated to advancing the science and clinical practice of radiosurgery; its members perform stereotactic radiosurgery in hospitals and freestanding centers throughout the world. Worldwide in 2009 there were 21,849 total treatments with CyberKnife, of which 9,896 were intracranial and 11,953 were extracranial treatments. In the United States, there were 14,619 total treatments with CyberKnife, of which 6,192 were intracranial and 8,427 were extracranial. UPMC Cancer Centers performed 451 intracranial treatments, ranking No. 1 in the world and No. 1 in the United States, and 189 extracranial treatments, ranking No. 11 in the world and No. 7 in the United States. The combined total of 640 CyberKnife treatments performed at UPMC Cancer Centers, however, earned the ranking of No. 1 both in the world and in the United States.

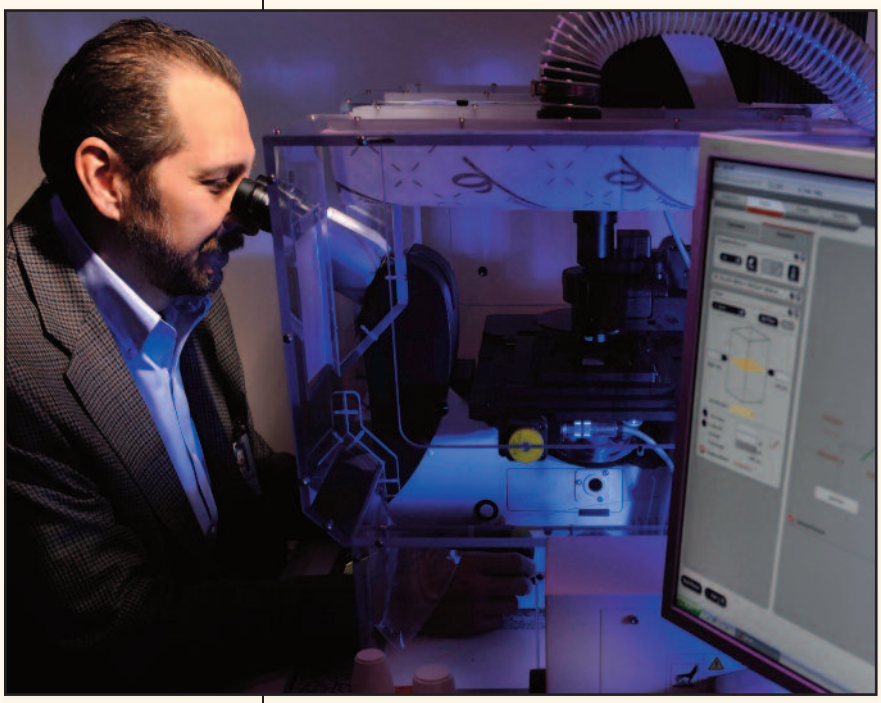
UPMC neurosurgeons and radiation oncologists reach milestone

UPMC's radiosurgical team recently performed their 10,000th Gamma Knife® radiosurgery, a milestone that further distinguishes UPMC as a world leader in radiosurgery experience. In 1987, L. Dade Lunsford, MD, distinguished professor of neurological surgery at the University of Pittsburgh and codirector, Center for Image-Guided Neurosurgery, UPMC, along with his radiation oncology partner, John C. Flickinger, MD, were the first clinicians in North America to use the Gamma Knife. The team, along with colleague Douglas Kondziolka, MD, worked with Gamma Knife designers and manufacturers to assist in the development of subsequent generations of Gamma Knife technology, which were pioneered at UPMC.

surgical oncology

Identifying BRAF gene may change surgery options

A recent study by lead investigator Linwah Yip, MD, a surgical oncologist at the UPMC Multidisciplinary Thyroid Center, has shown that identifying a specific gene mutation in certain thyroid cancer specimens may help doctors tailor surgery for patients with papillary thyroid carcinoma.



"For patients who have undergone surgery, BRAF testing can tell them if they have a high risk of their thyroid cancer coming back."

Linwah Yip, MD

The study, published in *Surgery* in December 2009, centered on the oncogene known as BRAF, which in a number of other studies has proven to be close to 100 percent predictive of thyroid cancer, according to Dr. Yip. "For that reason, using genetic testing to establish if a patient has BRAF-positive cancer prior to surgery can have important implications for the type and extent of surgery the patient needs," she explains. "BRAF-positive thyroid cancer patients should have the entire thyroid gland removed instead of having a partial thyroidectomy."

When patients present with a thyroid nodule at UPMC Cancer Centers, their biopsy specimens obtained through fine needle aspiration are routinely tested for an advanced panel of genetic markers, including the BRAF oncogene. Yuri Nikiforov, MD, PhD, also a physician-researcher at the University of Pittsburgh Cancer Institute (UPCI) and UPMC Cancer Centers, developed the panel and is one of the world leaders in thyroid cancer molecular marker research. This testing is important for patients both before and after surgery.

"BRAF tumors seem to be more aggressive," Dr. Yip explains. "For patients who have undergone surgery, BRAF testing can tell them if they have a high risk of their thyroid cancer coming back. This knowledge also is important before surgery, because those patients who are BRAF-positive may be predisposed to metastatic lymph nodes, so a surgeon might need to be more aggressive in evaluating the lymph nodes the first time around."

Dr. Yip sees great benefits for physicians who are able to offer their patients this advanced BRAF-mutation screening for papillary thyroid cancer. "To do a biopsy and get not only the confirmation of cancer, but also if the cancer has a tendency to be more or less aggressive based on the identified mutation can be of enormous help in making decisions about surgery and subsequent treatment, both from the surgeon's and patient's perspective," she says. "There has been controversy in thyroid surgery about what kind of lymph node dissection is needed — and BRAF testing could help guide this decision-making. We are hoping that molecular testing will ultimately help tailor the extent of initial surgery and limit the number of additional surgeries patients undergo."

At the UPMC Multidisciplinary Thyroid Center, all patient biopsies receive routine molecular testing. "To run the panel of tests, we must obtain the biopsy slides here because of how the specimens need to be processed," Dr. Yip adds.

For more information about BRAF testing, or to refer a patient to the UPMC Multidisciplinary Thyroid Center, call 412-586-9205, or e-mail Dr. Yip directly at yipl@upmc.edu.

PHP comparable to IHP for ocular melanoma, study finds

A recent clinical trial of patients with ocular melanoma that has metastasized to the liver has shown that the use of percutaneous hepatic perfusion (PHP) can provide antitumor efficacy comparable to isolated hepatic perfusion (IHP). In the study, led by James F. Pingpank, MD, a surgical oncologist at UPMC Cancer Centers and physician-researcher at the University of Pittsburgh Cancer Institute, patients who had been thought too advanced to treat actually responded well in the Phase III trial that had been given fast-track approval through the federal Food and Drug Administration.

Liver metastases are the sole life-limiting component of disease in the majority of patients whose ocular melanoma recurs. Because median survival after diagnosis of liver metastases is short and no satisfactory treatment options exist, Dr. Pingpank and investigators at the National Cancer Institute originally conducted trials to evaluate the use of IHP for these patients. IHP had significantly positive results, but subsequent treatments were not possible due to extensive scar tissue in the operative field upon recurrence of disease.

As the adjunct principal investigator for the Phase III trial, Dr. Pingpank worked with the manufacturer, Delcath Systems Inc., to design the PHP system, which uses a double balloon catheter inserted during a minimally invasive procedure to seal off the inferior vena cava above and below the liver instead of clamps to seal off the vena cava, hepatic artery, and gastroduodenal artery.

Once the liver is isolated and the blood inside the liver is removed, high-dose, heated chemotherapy is infused throughout the liver on a circuit utilizing charcoal filters to remove chemotherapy from the blood as it is returned to the patient. The results of the study showed that patients with liver-only disease responded well to the treatment.

More than half of patients who were previously thought to be too advanced to treat for ocular metastases to the liver can be treated with PHP and respond to the chemotherapy. In addition, they can be treated at multiple times, if needed, using this method. The determining factor for using PHP was the health of the liver, as patients whose serum bilirubin was greater than 2.5 generally are too sick to undergo the procedure.

For more information about PHP, please contact Dr. Pingpank at pingpankjf@upmc.edu.

UPMC surgical oncologist presents outcomes of robotic Whipple surgery at international pancreas symposium

A. James Moser, MD, codirector of the UPMC Pancreatic Cancer Center and UPMC surgical oncologist, presented an abstract on the minimally-invasive, robotic pancreatic duodenectomy (or Whipple procedure) at the Ninth World Congress of the International Hepato-Pancreato-Biliary Association held in April in Buenos Aires, Argentina. The conference drew surgeons from throughout North America, South America, and Europe. The minimally-invasive robotic Whipple program is the joint effort of Drs. Moser and Herbert Zeh III, MD, fellow codirector of the UPMC Pancreatic Cancer Center, with Kiran K. Turaga, MD, MPH, and David L. Bartlett, MD, chief, Division of Surgical Oncology, UPMC Cancer Centers. The team of Drs. Moser and Zeh has performed more than 40 robotic-assisted Whipple procedures at UPMC Cancer Centers, the highest number of any academic center in the world. They recently entered into a scientific partnership with Cleveland Clinic, which has performed about half as many robotic Whipples, to form the Minimally-Invasive Pancreas Surgery Consortium to share experiences and outcomes and expedite innovation in this rapidly evolving field.

For more information about the robotic Whipple procedure, or to discuss the team's clinical research or patient care opportunities, please contact Drs. Moser or Zeh at 1-888-623-PANC (7262) or visit the UPMC Pancreatic Cancer Center at www.UPMC.com.

The team of Drs. Moser and Zeh has performed more than 40 robotic-assisted Whipple procedures at UPMC Cancer Centers, the highest number of any academic center in the world.

UPMC
Cancer Centers

UPMC Cancer Centers and University of Pittsburgh Cancer Institute

Nancy E. Davidson, MD
Director

James T. Terwilliger
Executive Vice President

UPMC Cancer Pavilion
5150 Centre Ave.
Pittsburgh, PA 15232
412-647-2811

UPMC has consistently received national recognition from *U.S. News & World Report* magazine for offering one of America's top cancer programs. For more information about UPMC Cancer Centers' clinical services, or University of Pittsburgh Cancer Institute research, call **1-800-533-UPMC** or visit **www.UPMCCancerCenters.com**.

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>>> more medical oncology news

Tumor-associated virus may be the key to the immunologic understanding of other cancers

Two years ago, University of Pittsburgh Cancer Institute (UPCI) physician-researchers Patrick S. Moore, MD, MPH, American Cancer Society professor of microbiology and molecular genetics at the University of Pittsburgh School of Medicine and director of the Cancer Virology Program at UPCI, and Yuan Chang, MD, American Cancer Society professor of pathology, also at UPCI, identified a previously unknown virus, Merkel cell polyomavirus (MCV), and linked it with a rare but deadly skin cancer, Merkel cell carcinoma. Since that discovery, this husband-and-wife research team has advanced the understanding of the virus with the ultimate goal of targeting virus-induced cancers for treatment.

During investigation, Drs. Moore and Chang found that among most tumors positive for Merkel cell carcinoma, tumor cells were infected and expressing viral oncogenes, which caused cell proliferation. The virus infecting the cells, identified by Drs. Moore and Chang as MCV, showed a clonal integration, demonstrating that the cell was infected with the virus prior to becoming a tumor, a genetic signature for virus-associated cancers. According to Drs. Moore and Chang, MCV causes 80 percent of Merkel cell carcinoma cases.

MCV is the second human tumor virus found by this team — they previously isolated the Karposi's sarcoma-associated herpes virus (KSHV) — and only the seventh human tumor virus to be discovered. "While there is no specific treatment for MCV infection, identifying the agent and understanding how it triggers disease could lead to targeted interventions," says Dr. Moore.

In pursuit of that goal, the research team has developed a monoclonal antibody that allows them to determine if the virus is present in the tumor and expressing the protein that promotes cancer formation. Drs. Moore and Chang have used the antibody to survey tissue samples, including tumors, and have found the antibody specific for Merkel cell carcinoma.

Furthermore, they developed a serologic assay to see who carries MCV antibodies. "Using this assay, those patients who have Merkel cell carcinoma have a very high antibody pattern to the virus; whereas other control groups have a much lower antibody level," says Dr. Moore.

These discoveries have allowed Drs. Moore and Chang to gather some insight into how the virus moves and who it affects, important keys to understanding, treating, and preventing Merkel cell carcinoma. "By pursuing this, we hope to learn more about the natural history of the cancer and how we can intervene," says Dr. Chang.

Moving forward, Drs. Moore and Chang will continue to advance the groundwork they established to understand and treat the aggressive and often chemo-resistant form of skin cancer. "We have made initial inroads into this two-prong attack," says Dr. Chang. "We will continue to do basic research and we will continue to develop the translational aspects of our research."

If you are interested in enrolling a patient in Drs. Moore and Chang's Merkel cell carcinoma study group, or for more information on the work being done by these two researchers, visit www.tumorvirology.pitt.edu.

>>> more radiation oncology news

Fellow gives key plenary session talk at annual ACRO meeting

A third-year medical student completing a one-year National Institutes of Health fellowship with the Department of Radiation Oncology delivered one of only five plenary presentations at the 20th Annual Meeting of the American College of Radiation Oncology this past February. Jean-Claude Rwigema's presentation highlighted findings from a retrospective analysis by the department, which evaluated the relationship between tumor volume and radiosurgery dose to predict treatment outcomes in previously-irradiated patients with recurrent squamous cell carcinoma of the head and neck treated with stereotactic body radiotherapy (SBRT), a novel technique using stereotactic principles to perform "bloodless" surgery by delivering highly precise ablative doses of radiation. The study evaluated 96 patients treated between 2003 and 2008 and found that smaller tumor volume and higher doses were associated with improved outcomes with minimal treatment-related side effects. Under the direction of head and neck surgeon Robert L. Ferris, MD, and radiation oncologists Dwight E. Heron, MD, FACRO, and Steven Burton, MD, the research team developed a unique prediction model to assist clinicians in dose selections and prediction of outcomes in patients with very challenging disease recurrence. A Phase II trial at UPCI evaluating this approach using cetuximab, a targeted agent, with SBRT is nearing completion. The investigators have planned to further investigate the results in a randomized Phase III trial evaluating cetuximab and other chemotherapy agents in combination with SBRT.

If you have a patient who may be a candidate for this type of treatment and would like more information about this study, contact Dr. Heron at herond2@upmc.edu.