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REPORT TO PHYSICIANS
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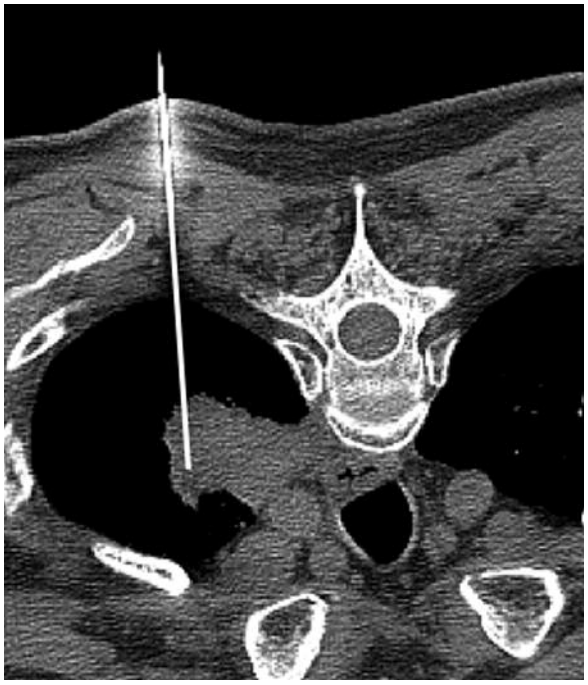
OncoLog

The BATTLE Results Are In

Phase II trial reveals molecular signatures in lung cancer that may guide treatment decisions.

By John LeBas

Non-small cell lung cancer (NSCLC), like so many other malignancies, does not represent a molecularly homogeneous group of tumors. Rather, NSCLC exhibits a wide range of mutations that should make it possible to choose treatment based on an individual tumor's molecular characteristics.



In the BATTLE trial, non–small cell lung cancers were biopsied upon patients' entry into the study and tested for a variety of biomarkers.

But the potential of customized treatment for NSCLC has been hampered by a lack of clinical data supporting the use of targeted agents, which shut down cancer through specific molecular interactions rather than broad cytotoxicity. To address this problem, researchers at The University of Texas M. D. Anderson Cancer Center launched a 3-year study of molecular characteristics and response to four targeted therapies in NSCLC.

The results, presented this spring at the plenary session of the American Association for Cancer Research's annual meeting, showed for the first time that real-time biopsies of NSCLCs reveal molecular signatures that may be able to predict which targeted therapies are most likely to work. The phase II clinical study, known as BATTLE, opens the door for increased treatment efficacy and better controlled clinical testing, investigators said.

"These molecular signatures, known as biomarkers, are a product of mutations and other cell abnormalities responsible for the cancer," said Edward S. Kim, M.D., an associate professor in the Department of Thoracic/Head and Neck Medical Oncology and principal investigator for the BATTLE (**B**iomarker-integrated **A**pproaches of **T**argeted **T**herapy for **L**ung Cancer **E**limination) study. "The targeted agents we tested are known to work against specific mutations. By identifying our patients' tumor biomarkers and evaluating their response to the targeted agents, we were able to determine a predicted therapy response based on biomarkers."

The data from BATTLE, which opened in 2006 and closed last fall, are also expected to help researchers design strategies for future clinical studies.

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The BATTLE Results Are In

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Impetus

Predicting a response to any given cancer therapy is important because the effectiveness of treatment often determines long-term prognosis. Targeted agents, in contrast to chemotherapy, do not work broadly against cancer cells; thus, in targeted therapy, knowing the molecular abnormalities of the tumor takes on even greater importance.

For some other cancers, such as colorectal cancers, targeted agents are being used effectively because biomarkers have been established through clinical testing. BATTLE is believed to be the first clinical trial to aimed at developing a panel of biomarkers for NSCLC in a real-time fashion. "Only in the past few years have we begun to understand the molecular mechanisms of lung cancer and relate them to therapy," Dr. Kim said. "Ultimately, we would like to be able to screen patients for tumor characteristics and give them appropriate therapies up front."

The testing approach used in BATTLE is a break from the traditional clinical trial design for lung cancer drugs, Dr. Kim said. "Typically, new agents are added to older chemotherapies and tested, but often the benefit in less than optimal," he explained. "We wanted to focus on the patient, rather than the drugs, to learn how individual tumor characteristics might lead to improved therapy." The trial also employed adaptive randomization, in which early results in patients are used to guide subsequent treatment assignments in the study.

"Ultimately, we would like to be able to screen patients for tumor characteristics and give them appropriate therapies up front."

— Dr. Edward S. Kim

Study details

All the study subjects had metastatic NSCLC that was refractory to chemotherapy, and each underwent a biopsy upon enrollment. Pathologists in a research laboratory checked the tumor samples for 11 biomarkers, such as overexpressed proteins representing known molecular pathways to cancer.

In all, 255 patients were randomly assigned to receive one of four promising targeted regimens: erlotinib (Tarceva), sorafenib (Nexavar), vandetanib (Zactima) and erlotinib with bexarotene (Targretin). Following treatment, patients were assessed for disease control, and statistical analysis was used to determine which biomarkers were associated with effective therapy.

Each of the four regimens was found to produce a better response than the other three for certain groups of patients. "There were some expected results and some surprises," Dr. Kim said. For example, as expected, patients who showed mutations of the epidermal growth factor receptor (EGFR) benefited most from erlotinib, an EGFR inhibitor. But surprisingly, patients who had a KRAS mutation benefited most from sorafenib, a drug used to treat kidney and liver cancer but with previously unknown effects in lung cancer.

Impressively, at the end of 8 weeks, 46% of patients in the trial were experiencing disease control. In contrast, the typical 8-week disease control rate for metastatic lung cancer treated with standard therapies is only about 30%. Median overall survival was 9 months, and side effects were tolerable.

Upcoming

While encouraging, the results from BATTLE must be confirmed in larger phase III trials, Dr. Kim said.

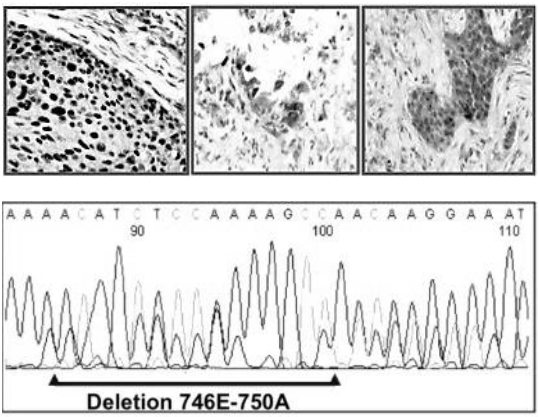
Future trials in the BATTLE program, which is funded by a U.S. Department of Defense grant, will focus first on untreated patients diagnosed with metastatic lung cancer, followed by patients with locally advanced cancer. Finally, if results continue to be positive, testing could be extended to patients

BATTLE Schema: Profiling Tumors to Develop Personalized Therapy

UMBRELLA PROTOCOL
To be eligible for the trial, patients had to have previously treated NSCLC, adequate performance status, and biopsy-amenable disease

CORE BIOPSY
Patients underwent tumor biopsy before further treatment

BIOMARKER ANALYSIS
Based on tumor characteristics, patients were placed in one of four biomarker groups: EGFR, KRAS/BRAF, VEGF, and RXR/Cyclin D1



Biopsy samples collected for BATTLE were examined by histology (above), gene sequencing (below, showing an EGFR gene mutation), and other methods. The data revealed that non–small cell lung cancers have molecular signatures that may be used to guide therapy.

with completely resected lung cancers, Dr. Kim said.

"Even in patients who are considered cured, there is a chance the tumor could return," he said. "But if we can test these patients for biomarkers, it may be possible to give them therapy that would prevent the cancer from recurring. If so, the ultimate result of BATTLE may be lung cancer prevention." ●

More detailed BATTLE results were reported at the American Association for Cancer Research's 2010 meeting. For information, visit www.aacr.org or www.mdanderson.org.

TREATMENT
Patients were assigned to receive erlotinib, vandetanib, erlotinib + bexarotene, or sorafenib; the primary endpoint was 8-week disease control

Shark Cartilage Compound Proves Ineffective in Lung Cancer

A shark cartilage extract developed as an anti-cancer agent had no effect on survival when combined with standard therapy for advanced non–small cell lung cancer (NSCLC), researchers recently reported.

The results of an international phase III clinical trial of the agent, AE-941 (Neovastat), cast doubt on the cancer-fighting efficacy of shark cartilage products. "We have absolutely no data showing improvements in survival, tumor shrinkage, and/or clinical benefits to patients from these products," said Charles Lu, M.D., an associate professor in M. D. Anderson's Department of Thoracic/Head and Neck Medical Oncology and the study's national principal investigator.

The trial, supported by the U.S. National Cancer Institute, was the first large, randomized clinical trial to test the anti-cancer benefits of shark cartilage. The absence of blood vessels in cartilage and low incidence of cancer in sharks had driven the hypothesis that shark cartilage might contain cancer-inhibiting compounds, researchers noted.

"These findings have to cast major skepticism on shark cartilage products that are being sold as cancer-fighting agents."
— Dr. Charles Lu

Various over-the-counter products developed from shark cartilage have been marketed as having therapeutic effects against cancer (although AE-941 has never been available over-the-counter). The trial was intended to address "the widespread use of poorly regulated complementary and alternative medicine products, such as shark cartilage–derived agents, among patients with advanced cancer, a population likely to be vulnerable to unsubstantiated marketing claims," the authors wrote.

In the trial, 379 patients—including 60 at M. D. Anderson—with untreated, unresectable stage III NSCLC were randomly assigned to receive AE-941 or placebo in addition to standard chemoradiation therapy. There was no significant difference in median overall survival (14.4 months for patients who received AE-941 vs. 15.6 months for patients who received placebo). Differences in median progression-free survival, time to progression, and tumor response rates were also insignificant.

"Clearly, these results demonstrate that AE-941 is not an effective therapeutic agent for lung cancer," Dr. Lu said. "So, too, these findings have to cast major skepticism on shark cartilage products that are being sold for profit and have no data to support their efficacy as cancer-fighting agents."

The results, first presented at the 2007 annual meeting of the American Society of Clinical Oncology, were published online in May in the *Journal of the National Cancer Institute*. ●

Endoscopic Repair of Colon Perforations

Nonsurgical techniques for closing gastrointestinal defects may yield benefits for patients undergoing colonoscopy.

By John LeBas

When Gottumukkala S. Raju, M.D., first began experimenting with a nonsurgical method of repairing colon perforations, there was virtually no U.S. experience with such an approach and only a rudimentary technique. He and his colleagues had to develop a system essentially from scratch, not knowing whether it would ever prove useful.

More than a decade later, following extensive experiments in laboratory animals and preliminary application in human patients, Dr. Raju has shown that the endoscopic perforation closure method can offer an alterative to surgery. With further refinements, invasive repair of colon perforations—a major complication of colonoscopy—may largely become a thing of the past, he said.

"Perforations during colonoscopy are rare, but when they occur, the patient has to be sent to surgery to have the hole repaired," said Dr. Raju, a professor in The University of Texas M. D. Anderson Cancer Center's Department of Gastroenterology, Hepatology and Nutrition, whose main interest is colon cancer prevention. "There are two main problems with this. One, you have to make a big hole in the abdomen to close a small hole in the colon. And two, it gives a lot of bad press to colonoscopies. If a person suffers a perforation, his family and friends may hear about it and never go in for colon cancer screening."

> **"We may eventually be able to eliminate surgery for most patients with difficult benign polyps."**
>
> **— Dr. Gottumukkala S. Raju**

Setting and early experiments

Perforations generally occur during colonoscopies as a result of the physician unintentionally puncturing the thin colon wall while manipulating the endoscope up through adhesions or scar tissue from prior abdominal surgeries, pelvic surgeries, or radiation, or while a polyp is being cut from the colon wall. Trying to remove large polyps, flat lesions, and residual polyp tissue that has become tethered to the colon wall with scar tissue following a previous removal attempt can also cause a perforation.

Because colonoscopies are essential in preventing colon cancer, Dr. Raju saw a need to limit the negative effects of perforations. It was the late 1990s, and while at a conference he came across a simple yet inspiring product: clips designed to stanch bleeding during endoscopic procedures.

"I thought to myself that these clips could probably be used to close perforations as well, but they would need to provide secure closure of the hole," he said. "So we began experimenting at The University of Texas Medical Branch at Galveston to see whether this could be done." The first successful experiments, reported in the early 2000s, showed proof of concept in pigs: the clips were able to be placed endoscopically, cinching down linear perforations up to 7 cm and resulting in leak-proof seals.

Encouraged by the results, Dr. Raju and colleagues made their next experiments tougher by trying to clip circular holes. Adjustments to the technique showed this could usually be done as well. For those holes that couldn't be clipped closed, a new suturing device developed by another researcher provided a successful alternative approach. A subsequent multicenter trial using animals showed that surgical and endoscopic perforation repair yielded similar outcomes but with fewer adhesions resulting from endoscopy.

More recent animal experiments conducted at The University of Texas Medical Branch at Galveston (with collaborators Ijaz Ahmed, M.D., and Guillermo Gomez, M.D.) involved removing sections of colon from animals and using clips or sutures to close the defect. These experiments were conducted to develop techniques to remove polyps that are tethered to the colon wall by removing a section of the wall and then closing the defect, all through an endoscope. The experiments also proved successful, with no resulting perforations or leaks.

Human application

Following the positive animal experiences, Dr. Raju was able to use the endoscopic repair techniques in people who were not candidates for surgery owing to comorbidities. In one patient, clips were used to close a gastric fistula following esophageal cancer surgery. Another patient—a woman with colon cancer who was obese and had a pul-

monary embolism—underwent endoscopic repair of a colon fistula to the skin. The patient's output from the fistula reduced from 100 cc per day to 5 cc per day immediately following closure, and the fistula healed after a few months without the need for surgery.

Application of these endoscopic closure techniques could help physicians attempt endoscopic resection of large polyps or flat lesions that are otherwise sent to surgery for fear of perforation, Dr. Raju said. "Hopefully, our next step is to test this procedure in patients who have benign colon polyps tethered to the colon wall that would be difficult to remove endoscopically, polyps that would otherwise require surgery," said Dr. Raju, who plans to collaborate with a laparoscopic surgeon. "If we can do a good job removing such polyps and repairing the defects endoscopically, we may eventually be able to eliminate surgery for most patients with difficult benign polyps." ●

For more information, contact Dr. Raju at 713-794-5073.

ADDITIONAL RESOURCES

For further reading about endoscopic closure of perforations, see the following review article written by Dr. Raju:

Raju, GS. Endoscopic closure of gastrointestinal leaks. *Am J Gastroenterol.* 2009;104:1315–1320

A DVD developed by Dr. Raju and colleagues is available from the American Society for Gastrointestinal Endoscopy. The DVD, titled "Endoscopic Closure of Gastrointestinal Leaks," discusses techniques and technologies used for nonsurgical gastrointestinal perforation closure. Visit the society's Web site, www.asge.org, for ordering information. Dr. Raju and his collaborators (Takuji Gotoda, M.D., and Hisatomo Ikehara, M.D., National Cancer Center, Japan; and Tonya Kaltenbach, M.D., and Roy Soetikno, M.D., VA Palo Alto Health Care System, Palo Alto, California) received the society's 2010 Audiovisual Award for the video. ●

IN BRIEF

Stem Cells Seen Repairing Heart Attack Damage Over Time

Researchers at The University of Texas M. D. Anderson Cancer Center recently used human adult stem cells to repair heart attack damage in mice, tracking the cells over time with novel imaging methods.

The study, with researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital, furthers the understanding of how stem cell repair works and how stem cells may be used therapeutically in humans, investigators said.

In early human clinical trials, injection of a patient's own adult stem cells into the heart has shown some efficacy in assisting recovery after a heart attack, said Edward T. H. Yeh, M.D., a professor in and chair of M. D. Anderson's Department of Cardiology and senior author of the current study.

"But nobody knows how the stem cells work or how long they last and function in the heart," Dr. Yeh said. "This study shows how one type of adult stem cell works."

The research team used adult stem cells characterized by the presence of CD34 protein on the cell surface. These CD34–positive cells usually differentiate into blood vessel cells, and earlier research by Dr. Yeh and colleagues showed that CD34–positive cells are also capable of becoming cardiomyocytes and smooth muscle cells.

After tying off an artery to induce a heart attack in the mice, the team injected CD34–positive cells around the damaged area. A series of experiments showed:

- The CD34–positive cells survived in the left ventricle of the heart for 12 months or longer.
- Left ventricular ejection fraction, a measure of how much blood is pumped from the heart to other organs at each contraction, improved in treated mice compared with controls for 52 weeks.

> "This study shows how one type of adult stem cell works in the heart."
>
> **— Dr. Edward T. H. Yeh**

- This improvement was the result of increased blood vessel formation in and around the injured area or paracrine signaling by the stem cells to other nearby cells rather than the formation of new heart muscle. Using an antibody technique developed by Dr. Yeh and colleagues, the team found that antibodies that blocked the formation of new blood vessels completely negated the treatment benefit while antibodies that blocked heart muscle cell formation had no effect.

The findings may have important implications for cancer care, since some chemotherapies weaken the heart, Dr. Yeh said. During chemotherapy treatment, oncologists closely monitor ventricular ejection fraction, one of the most important indicators of heart function. If the left ventricular ejection fraction drops past a certain value, chemotherapy is halted.

To observe the stem cells over time, researchers labeled them with a triple-fusion reporter gene that enabled their detection with three types of imaging. A retrovirus was used to deliver the reporter gene to the stem cells. This triple reporter vector was invented by senior co-author Juri Gelovani, M.D., Ph.D., a professor in and chairman of M. D. Anderson's Department of Experimental Diagnostic Imaging.

Researchers used bioluminescence imaging to study how long the injected stem cells survived in the heart. Positron emission tomography/computed

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tomography coupled with magnetic resonance imaging (MRI) pinpointed the stem cells' location in the heart muscle.

MRI also was used to measure ejection fraction and to assess the efficacy of the stem cell therapeutic approach for improving cardiac contractile function.

The study was reported online in May in the journal *Circulation Research*. ●

Additional Blood Data May Improve Pediatric Leukemia Predictions

Using absolute lymphocyte count (ALC) as a prognostic tool along with the minimal residual disease (MRD) indicator may allow more accurate predictions of treatment outcomes in young leukemia patients, researchers from the Children's Cancer Hospital at M. D. Anderson have found.

In a retrospective study reported at the American Society of Pediatric Hematology/Oncology's annual meeting, researchers concluded that ALC—obtained from a complete blood count—is at least as powerful as MRD in independently predicting prognosis for children with acute lymphocytic leukemia (ALL). MRD, for several years considered the best prognostic tool for pediatric ALL relapse, overlooks a subset of patients who are at a higher risk of relapse, said Patrick Zweidler-McKay, M.D. Ph.D., assistant professor and first author of the study.

The study was based on a review of 171 pediatric ALL patients. After a month of treatment, patients who were MRD–positive with a low ALC had an event-free survival rate of 33% and a 5-year overall survival rate of 41%. However, patients who were MRD–positive but with a high ALC had an event-free survival rate of 69% and a 5-year overall survival rate of 92%. Patients who were MRD–negative and had a high ALC had a 99% 5-year overall survival rate.

> "If we know that a patient is at a high risk of relapse from the beginning, then potentially we can adjust the treatment plan to a more aggressive therapy."
>
> **— Dr. Patrick Zweidler-McKay**

Using ALC, it may be possible to define which MRD–positive patients are at a higher risk of relapse, Dr. Zweidler-McKay said.

"Our ultimate goal is to use these prognostic tools in the future to guide treatments for our patients," he explained. "If we know that a patient is at a high risk of relapse from the beginning, then potentially we can adjust the treatment plan to a more aggressive therapy." ●

Pediatric Patients with Rare Tumor May Benefit from Heated Chemotherapy

A study at the Children's Cancer Hospital showed that an adult surgery adapted for use in young patients improved survival among children with a rare cancer of the abdomen.

The study, reported in May in the *Journal of Pediatric Surgery*, looked retrospectively at 24 pediatric patients with desmoplastic small round cell tumor (DSRCT). Those who received hyperthermic intraperitoneal chemotherapy (HIPEC or "heated chemotherapy") had a 3-year overall survival rate of 71%. Only 26% of patients who received standard treatment not involving HIPEC survived 3 years.

DSRCT is an aggressive soft-tissue sarcoma that typically presents as multiple tumors in the abdominal and pelvic areas. The disease most often occurs in young Caucasian males, with fewer than 200 cases being reported worldwide since 1989. The overall survival rate for DSRCT is approximately 30%–55%, in part owing to the disease commonly being resistant to chemotherapy and radiation therapy.

> "This technique is safe and advantageous for young patients who have multiple tumors in their abdomen."
>
> **— Dr. Andrea Hayes-Jordan**

Andrea Hayes-Jordan, M.D., an assistant professor and first author of the study, also attributes the poor outcomes to tumor cells being left behind after debulking surgery, allowing the cancer to spread in the abdomen and to other organs.

When using HIPEC for DSRCT, Dr. Hayes-Jordan first spends 10 to 12 hours removing tumors—which may number in the hundreds—from the patient's abdominal cavity. Then she runs the chemotherapy, heated to 104–106 F, throughout the cavity while the patient lies on a cooling blanket to keep the body temperature at a safe level. The chemotherapy kills any microscopic tumor that is left behind after the surgery. Within 1 to 2 months, patients often fully recover from surgery and resume regular activities.

Dr. Hayes-Jordan is believed to be the first and only surgeon in the country using HIPEC in children.

Patients reviewed in the study ranged in age from 5 to 43 years; those receiving HIPEC ranged from 5 to 25 years old. Results indicated that younger patients had better outcomes with HIPEC than patients older than 18 years. Disease-free survival was also better for those who received HIPEC in addition to debulking surgery. At 1 year, the disease-free survival rate was 14% for patients who received only surgery compared with 53% for those who also received HIPEC.

"This study demonstrates that the surgical technique is safe and advantageous for young patients who have multiple tumors in their abdomen," Dr. Hayes-Jordan said. "In the past, these patients were told there was nothing else to be done, but now we

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HOUSE•CALL

Skin Cancer Screening: What Is It and Who Should Get It?

Skin cancer is the most common form of cancer in the United States, with more than 1 million new cases diagnosed each year, according to the National Cancer Institute. Fortunately, the most common types of skin cancer can be effectively treated if diagnosed early enough. Skin cancer screening involves a quick and painless examination and is the first step in detecting all types of skin cancer early.

Types of skin cancer

Basal cell carcinoma, the most common type of skin cancer, often appears as a spot (growth) on the face, ears, scalp, or neck that will not heal. The spot may bleed from even mild trauma, such as drying with a towel. **Squamous cell carcinoma,** the second most common type of skin cancer, usually affects middle-aged and elderly people. It occurs as a new or enlarging spot that may bleed or cause pain. **Melanoma,** the third most common type of skin cancer, appears as a new mole or as an existing mole that has changed in size, shape, or pigmentation. The lesion will usually have a ragged border and may bleed, itch, or cause pain.

Left untreated, skin cancer may spread on the surface of the skin or to other parts of the body. Basal cell carcinoma tends to grow larger on the skin and spread to the structures underneath, while squamous cell carcinoma may spread to nearby lymph nodes. Melanoma, the most dangerous type of skin cancer, may spread to the lungs, liver, bones, or brain.

Who should be screened?

The following factors increase a person's risk of skin cancer:

- Age of 50 years or older (for men)
- Light skin
- Green or blue eyes
- Living close to the equator
- A personal or family history of skin cancer
- Exposure to ultraviolet light, ionizing radiation, or certain chemicals

Ana Mercedes Ciurea, M.D., an assistant professor in The University of Texas M. D. Anderson Cancer Center's Department of Dermatology who performs skin cancer screenings at M. D. Anderson's Cancer Prevention Center, recommends that people without risk factors for skin cancer be screened once a year. Those who have risk factors may need to be screened every 6 months. Patients with a history of skin cancer may need to be screened more often, depending on the type of cancer and how long ago it occurred. A physician can advise the best screening schedule to follow.

Dr. Ciurea added that people should examine their own skin once a month in the mirror. "We need to get in the habit of looking at our skin and knowing it," she said. Changes in the skin should be brought to a doctor's attention.

What to expect

Screening for skin cancer is a straightforward process. During a routine screening appointment at M. D. Anderson's Cancer Prevention Center, the patient first discusses the reason for the visit with a nurse, who shows the patient a brief video about the types of skin cancer. The patient then changes into a hospital gown, and a doctor examines the patient from the top of the head to the soles of the feet, classifying each mole or lesion and explaining its cause to the patient. The doctor may remove growths called actinic keratoses, which are caused by sun damage and sometimes develop into squamous cell carcinoma, by freezing them with liquid nitrogen. At the patient's request, the doctor may also remove benign moles for cosmetic reasons. A typical appointment takes less than an hour.

Self-examination: Check your skin regularly and tell your doctor about any suspicious changes.

If the doctor sees a lesion that appears malignant, he or she will most likely remove a small sample for further testing. This can be done during the screening visit and requires only a local anesthetic and a small incision. The specimen will be sent to a pathologist at M. D. Anderson, who will determine whether the lesion is malignant and, if so, the type of cancer. Results are typically available in 7 to 10 days, and if necessary, a follow-up appointment is scheduled when the patient learns the results. Dr. Ciurea said the patient is provided with a call-back number in case questions arise before the follow-up appointment.

Usually, a skin cancer screening will reveal no signs of cancer, giving the patient peace of mind. And when a problem is detected, the screening process has given the patient the best chance of successfully treating a potentially serious condition. ●

For more information, talk to your physician, or:

- *Call M. D. Anderson's Cancer Prevention Center at 1-800-438-6434*
- *visit www.mdanderson.org*
- *call* askMDAnderson *at 1-877-632-6789*

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IN BRIEF

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can add months and often years to their lives using this surgery.

"We're sharing this technology with other centers so that they will also be able to help such children. In the years to follow, we hope to try different chemotherapies with the procedure to better the outcomes and decrease any toxicities."

Dr. Hayes-Jordan said she hopes that the data from the study will encourage more centers to begin performing HIPEC on pediatric patients with abdominal tumors. She also plans to extend the study to include other cancers that metastasize to the abdomen. ●

New Findings Refute Link Between UVA, Melanoma

Exposure to ultraviolet A (UVA) light in early life does not cause melanoma in a fish model, contrary to earlier findings from the same fish model, M. D. Anderson scientists recently reported.

UVA exposure is unlikely to have contributed to a rise in the incidence of melanoma over the past 30 years, the researchers concluded, because the fish model had been the only animal model to indicate a connection between exposure to UVA at a young age and later development of melanoma.

"Our data refute the only direct evidence that UVA causes melanoma, which is not to say that UVA is harmless," said David Mitchell, Ph.D., a professor in M. D. Anderson's Department of Carcinogenesis and lead author of the study. "UVA is just not as dangerous as we thought because it doesn't cause melanoma."

Dr. Mitchell and colleagues tested the effects of UVA and ultraviolet B (UVB) light exposure in melanoma-prone fish hybrids. UVB exposure induced melanoma in 43% of exposed fish, compared with 18.5% in a control group that received no UV exposure and only 12.4% of fish exposed to UVA.

An influential 1993 study using the same hybrid fish connected UVA exposure to melanoma. Until that study, Dr. Mitchell said, sunscreens protected only against UVB exposure; however, UVA makes up 90% of the ultraviolet spectrum of sunlight.

"The thought was that people who used sunscreen stayed out in the sun longer, absorbing a higher dose of UVA, causing a higher risk for melanoma," Dr. Mitchell explained.

Most sunscreens now protect against UVA, and the increase in melanoma incidence has been thought to be partly attributable to childhood exposure to UVA back when sunscreens blocked only UVB. That's unlikely, given the new results, Dr. Mitchell said.

The findings were reported online in May in the *Proceedings of the National Academy of Sciences*. ●

Visit www.mdanderson.org/newsroom for more information.

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