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REPORT TO PHYSICIANS

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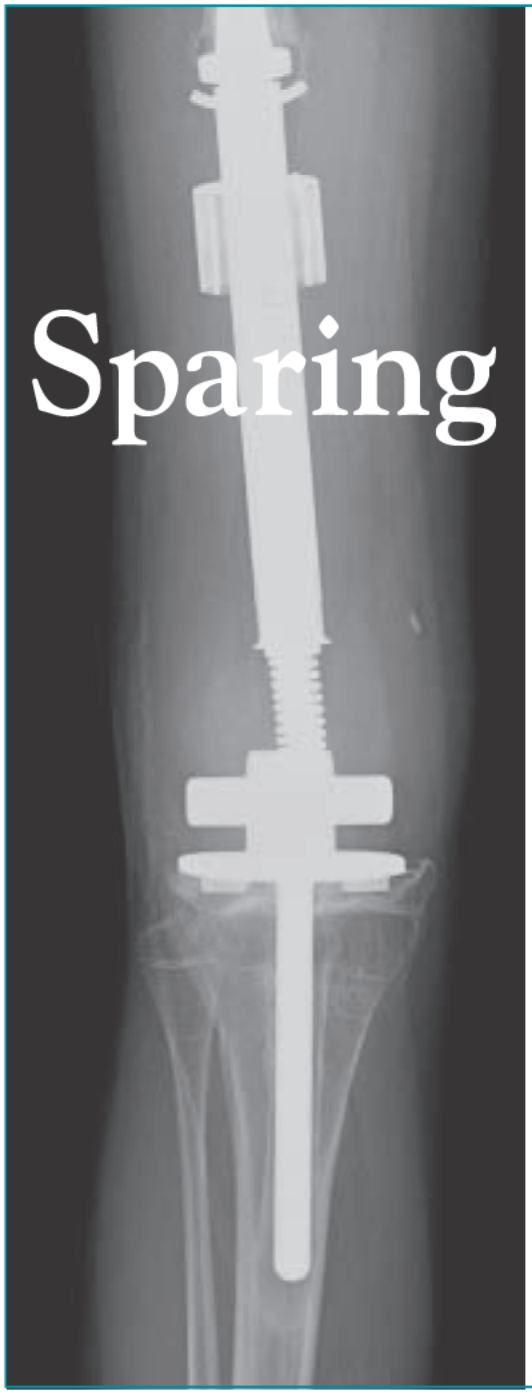

Advances in prostheses and surgery help patients with bone cancer avoid amputation.

Sparing Life and Limb

By Sunni Hosemann

J[redacted] clear blue eyes twinkle and she breaks into a big smile as a text message appears on her cell phone. With an impish grin, she "texts" back with the dexterity that only a 13-year-old could manage. She's the picture of an all-American teen: a sweet and somewhat shy smile, freckles, a ponytail, blue jeans, sneakers, and a T-shirt. But what one wouldn't know just by looking at her is that, thanks to advances in limb-sparing technology, [redacted] is lucky to have her own leg.

At age 11, [redacted] began experiencing pain in her knee when she was playing softball. Perhaps a strain or an injury? It began to bother her more. Growing pains, maybe? It became more noticeable. An X-ray delivered bad news: [redacted] had a tumor—an osteosarcoma—in her knee.

In another time and another place, [redacted] would have required an above-the-knee amputation of her leg. Even today, she might have been spared the amputation but could have faced a dozen or more additional surgeries by the time she reached adulthood. Instead, physicians used a novel implanted prosthesis that "grows" with [redacted]—without follow-up surgery—to replace the diseased bone. *(Continued on* page 2*)*

This bone-replacing prosthesis provided an alternative to above-the-knee amputation for treatment of an osteosarcoma. The device has a locked spring mechanism that allows it to "grow" along with the patient.

THE UNIVERSITY OF TEXAS
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Sparing Life and Limb

(*Continued from* page 1)

Alternatives to amputation

For some time now, orthopedic surgical oncologists have been able to perform limb-salvage surgery using a variety of ingenious techniques and advanced prostheses that allow optimal function after removal of diseased bone. Depending on the size and location of the resulting defect, bone can be replaced by an endoprosthesis (an internal prosthesis usually made of metal), an autograft (bone transplanted from another area), or less commonly, an allograft (bone from a cadaver). "The technology behind prostheses for bones and joints is constantly improving," said Christopher Cannon, M.D., an orthopedic surgeon who is assistant professor in the Department of Orthopaedic Oncology at The University of Texas M. D. Anderson Cancer Center. "This translates into better function for patients." [redacted] is the recipient of one of the latest advances in such technology.

Special challenge: patients who are still growing

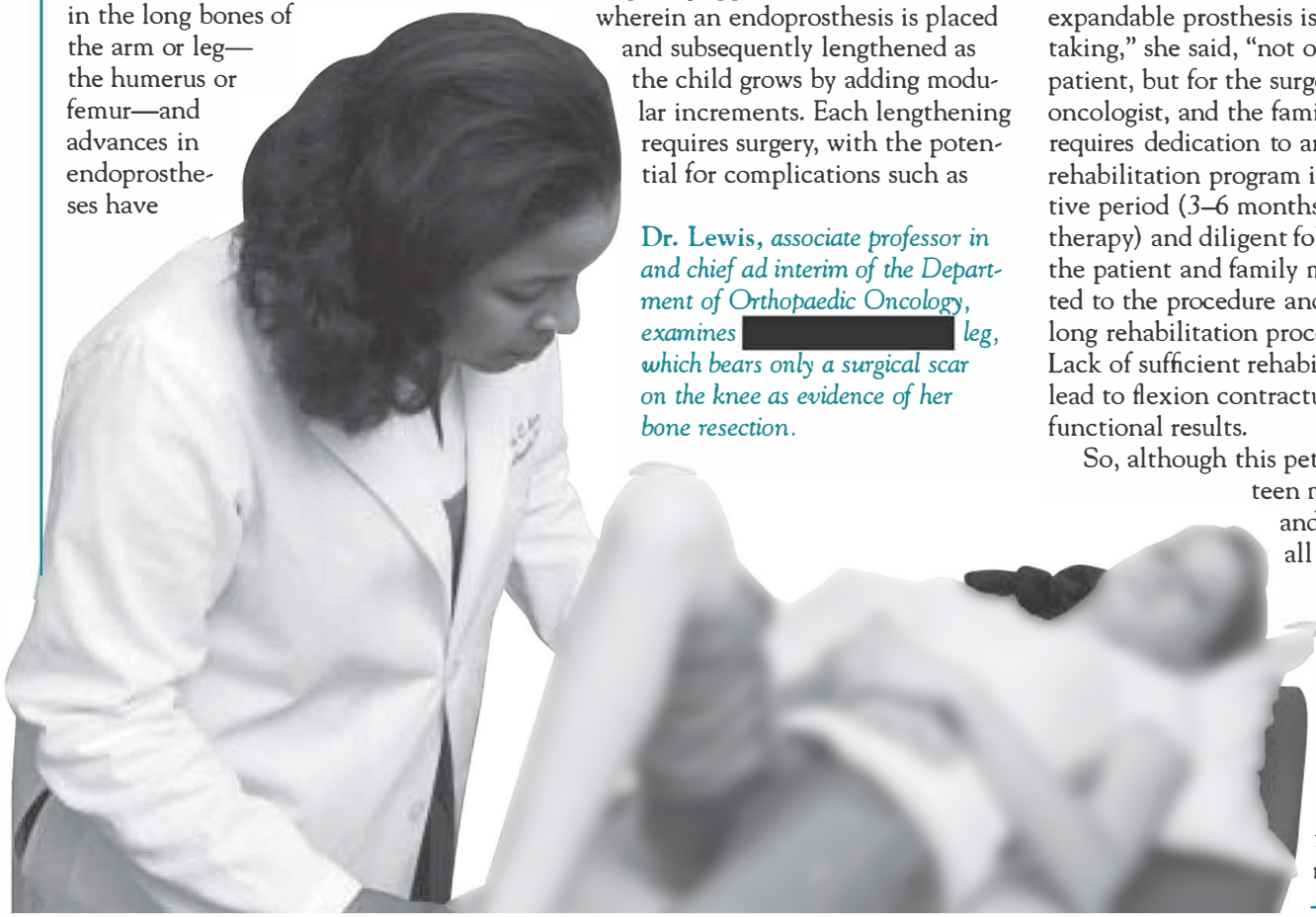
Many bony tumors occur in the long bones of the arm or leg—the humerus or femur—and advances in endoprostheses have allowed patients to keep their own limbs. In an adult, it's a matter of replacing the lost bone with a prosthesis suited to size and function. However, the most common tumors of the bone---osteosarcoma and Ewing sarcoma—frequently occur in children or adolescents who have not achieved full growth, and frequently these tumors occur in a location—the ends of long bones—that makes it impossible to spare the growth plate. According to Valerae Lewis, M.D., an orthopedic surgeon who is associate professor in and chief ad interim of the Department of Orthopaedic Oncology, in the past, even where a prosthesis could be put in place to spare the current limb, continued growth resulted in an unacceptable outcome: a dysfunctional growth discrepancy between the affected and unaffected limbs. In the case of a leg, this produced gait abnormalities that were obvious and untenable. Therefore, if a child had any significant growth left, amputation was the preferred treatment.

More recently, surgeons have used a limb-sparing approach in these children wherein an endoprosthesis is placed and subsequently lengthened as the child grows by adding modular increments. Each lengthening requires surgery, with the potential for complications such as infection. With this approach, a child might have 8–20 additional surgeries before reaching full growth, at which time a more permanent prosthesis would be placed.

Clearly, a prosthetic device that could accommodate growth was needed. For [redacted], Dr. Lewis used just such a device: it is a prosthesis that expands without additional surgery. The Repiphysis she used has a locked spring mechanism that allows controlled expansion of the prosthesis using an external electromagnetic device. [redacted] has undergone two expansions so far. Expansion increments are between 1 and 2 cm, and expansions are done under general anesthesia. Eventually, expansion may be done as an outpatient procedure, but for the near term, [redacted] will be admitted to the hospital overnight.

[redacted] mother, [redacted], considers herself fortunate to have found Dr. Lewis to treat her daughter. But for [redacted] to have received this procedure, more than luck was involved. According to Dr. Lewis, candidates for this procedure must be chosen carefully. "Any expandable prosthesis is a large undertaking," she said, "not only for the patient, but for the surgeon, the medical oncologist, and the family." Success requires dedication to an aggressive rehabilitation program in the postoperative period (3–6 months of physical therapy) and diligent follow-up. "Both the patient and family must be committed to the procedure and a relatively long rehabilitation process," she said. Lack of sufficient rehabilitation can lead to flexion contractures and poor functional results.

So, although this petite, ponytailed teen may be smiling and "texting" like all her friends, she has had to work at her recovery with a dedication not often demanded of someone her age, and her family also has made a consider-



Dr. Lewis, *associate professor in and chief ad interim of the Department of Orthopaedic Oncology, examines* [redacted] *leg, which bears only a surgical scar on the knee as evidence of her bone resection.*

> **"Any expandable prosthesis is a large undertaking, not only for the patient, but for the surgeon, the medical oncologist, and the family."**
>
> **– Dr. Lewis**

able commitment to her recovery process. The reward: except for the surgical scar on her knee, her right leg looks just like her left leg.

Other challenges

Although most occur in the long bones, bone tumors do affect other locations and often call for other approaches when prostheses are not feasible, according to Dr. Lewis. One of her patients was a young woman who lost a significant portion of her pelvis to osteosarcoma; Dr. Lewis used the patient's own fibula to construct a stabilizing hip scaffold. The woman recently gave birth.

Often, Dr. Lewis elects to use the patient's fibula to replace a humerus and thus leave the patient with a functional and growing humerus. Using the patient's own bone has distinct advantages: it is alive, it is vascularized, and when the physis is included, it maintains the ability to grow.

Sometimes, tumor size or location requires yet more innovation: Dr. Lewis has also created functional knee joints from ankles using a procedure called rotationplasty wherein the entire tibia, with nerve bundles intact, is rotated 180 degrees and reattached to the fibula, with the ankle joint becoming the new knee. In essence, this creates an amputation below the knee, which is far more favorable for the patient than an above-the-knee resection, and thus is a useful technique when sparing of the full limb is not possible. The procedure is a modification of a technique first described by J. Borggreve in 1930 for limb shortening and knee ankylosis secondary to tuberculosis. Patients who have this procedure do require a lower-limb prosthesis for bipedal ambulation but have been found able to walk for longer periods of time than those fitted with prostheses above the knee. Although the result is less aesthetically pleasing than that achieved by internal prostheses, these patients—unlike those with an endoprosthesis—are able to participate in vigorous, high-impact sports.

When the epiphysis (and therefore the growth plate) is not affected by the tumor, still other options exist for resecting the tumor and filling the resulting defect with bone, either by grafting it from other sites or by techniques like distraction osteogenesis, where the remodeling process seen in healing bone is put into use by transporting small (1 mm) segments of bone from an osteotomy in the same bone to gradually fill in the defect.

Limb-sparing procedures are very much customized to the patient based on the size and location of the tumor, the lifestyle and growth potential of that individual, and the patient's desire and ability to handle the demands of recovery. A potential candidate for limb-sparing surgery should be evaluated by an orthopedic oncologist familiar with limb-sparing options, and this should happen before any biopsy is done, as some biopsy techniques may limit reconstructive options. Advances in imaging techniques have been critical to the success of this surgery, as it is now possible to better delineate tumor margins during treatment planning.

All of these procedures require more skill on the part of the surgeon—and more dedication on the part of the patient—than do amputations, but for young patients like [redacted] the importance of having her own leg may be hard for the rest of us to calculate. ●

For more information on limb-salvage surgical procedures, call Dr. Lewis at 713-792-5073. To refer a patient, visit www.mdanderson.org/departments/ortho/.

IN BRIEF

Second-line CML Drug Shows Promise as First-line Therapy

Researchers at M. D. Anderson Cancer Center recently reported that nearly all patients taking dasatinib as a first-line therapy for chronic myelogenous leukemia (CML) had a complete cytogenetic response within a year of beginning treatment.

Dasatinib is traditionally used as a second-line therapy for CML, but researchers found that it has high rates of rapid response when used as a first-line therapy in patients newly diagnosed with the disease. The findings were reported at the American Society of Clinical Oncology annual meeting in June.

"We are starting to see very good responses very early with this treatment," said Jorge Cortes, M.D., professor in the Department of Leukemia and senior investigator on the study. "These results appear to be better than what we see after the same amount of time with the standard first-line drug, imatinib."

The phase II trial evaluated 31 patients between November 2005 and December 2006. Patients were randomly assigned to receive dasatinib at either 100 mg once daily or 50 mg twice daily. Dr. Cortes and his colleagues noted a complete cytogenetic response, or complete disappearance of the chromosomal abnormality that causes CML, in 77% of evaluable patients at 3 months, 92% at 6 months, and 95% at 1 year. Results for the two dosing regimens were similar.

These responses compare favorably with earlier data on imatinib: at 6 months, complete response rates are 54% at 400 mg daily and 85% at 800 mg daily, and at 12 months, complete response rates are 72% at 400 mg and 92% at 800 mg. Furthermore, the side effects of dasatinib were low grade and manageable in all patients, and there was less toxicity in these patients than in CML patients taking imatinib, according to Dr. Cortes.

(Continued on page 6*)*

Can a Common Spice B

Western science may be substantiating what E
that curcumin, the main ingredient of the curry s

By Dianne C. Witter

Razelle Kurzrock, M.D., rigorously evaluates the laboratory data behind any new pharmaceutical agent she considers moving into clinical trials at M. D. Anderson Cancer Center. As a physician, she is cautious; as a scientist, she's a skeptic; she wants unbiased, evidence-based information. And that, to her own surprise, is how she became interested in studying curcumin—the primary ingredient of the curry spice turmeric—as a possible anticancer agent in humans.

"Dr. Bharat Aggarwal, chief of the cytokine research laboratory in the Department of Experimental Therapeutics, came to me and said, 'I want to show you some great results we've gotten in the lab with an exciting new agent,'" said Dr. Kurzrock. "But he wouldn't tell me what the agent was—he wanted me to see the data first."

Dr. Kurzrock, professor in and chair ad interim of M. D. Anderson's Department of Investigational Cancer Therapeutics (formerly the Phase I Clinical Trials program), was impressed with the data. "It was clear that this agent was just as potent at killing tumor cells in the lab as any experimental drug I'd seen from pharmaceutical companies," she said. When Dr. Aggarwal told her this active agent was curcumin, she was intrigued and began designing a clinical study to test curcumin's efficacy in humans.

Shutting down the master switch

Curcumin's anti-inflammatory properties have been valued in Eastern medicine for centuries, but its specific mechanism of action has only recently been identified. In 1995, Dr. Aggarwal and colleagues demonstrated that curcumin shuts down nuclear factor kappa B (NF-κB), which is involved in the regulation of inflammation and many other processes.

By blocking the activity of this "master switch," curcumin appears to interfere with the cancer process at an early point, impeding multiple routes of development: reducing the inflammatory response, inhibiting the proliferation of tumor cells, inducing their self-destruction, and discouraging the growth of blood vessels feeding tumors. These effects can shrink tumors and inhibit metastasis. Furthermore, shutting down NF-κB can enable traditional chemotherapy drugs to destroy cancer cells more effectively.

Hundreds of laboratory studies by Drs. Aggarwal and Kurzrock and others have demonstrated that curcumin is biologically active against many types of cancer cells—melanoma, and breast, bladder, brain, pancreatic, and ovarian carcinomas, to name just a few. "In the lab, we haven't yet found a type of cancer it doesn't show activity against," Dr. Aggarwal said.

While it's a long road from lab to clinic, Dr. Aggarwal sees promise in curcumin both as a possible preventive agent and as a cancer treatment. As a medicinal agent, its potential extends far beyond cancer. Laboratory studies have demonstrated curcumin's promise in a number of different diseases that are also affected by inflammation, including arthritis, inflammatory bowel disease, Alzheimer's disease, diabetes, cardiovascular disease, autoimmune diseases, and others. In light of these findings, the number of clinical studies of curcumin has grown substantially in the past few years and continues to rise.

Dr. Aggarwal *is conducting laboratory studies on of curcumin, which is the main ingredient of the cu*

Studying activity in cancer patients

The clinical research on curcumin in cancer is new but promising. Early studies at M. D. Anderson and elsewhere have shown curcumin to be well tolerated and non-toxic at high oral doses.

Dr. Kurzrock and colleagues recently conducted a trial of curcumin in 49 patients with advanced pancreatic cancer, which is notoriously resistant to treatment. Two of those patients had clinically meaningful responses and remained stable for 8 months and more than 22 months, respectively. Another had a brief but dramatic response (73% reduction in tumor size).

"In advanced pancreatic cancer, the response rate to the Food and Drug

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astern medicine has maintained for centuries—
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> **Dr. Bharat Aggarwal came to me and said, 'I want to show you some great results we've gotten in the lab with an exciting new agent.' But he wouldn't tell me what the agent was—he wanted me to see the data first."**
>
> **– Dr. Kurzrock**

Dr. Kurzrock *is designing clinical trials of curcumin, based on promising lab results.*

Administration-approved treatments is only about 5%, so we were very encouraged that we saw any activity at all in this group," said Dr. Kurzrock. "That tells us curcumin does have biologic activity in pancreatic cancer—there was a true antitumor effect. It's too soon to know if it will affect survival rates, but more study is definitely warranted." The fact that some patients benefited is encouraging, since there were questions about whether therapeutic concentrations could be achieved with oral administration.

To address the issue of absorption, Dr. Kurzrock is leading the development of an intravenous, liposome-encapsulated delivery system for curcumin that she says has so far been "very potent" in the lab. Liposomal curcumin would be given intravenously, thereby circumventing the problem of poor absorption.

"The fact that the curcumin did show some activity in the study even though it was poorly absorbed suggests that if we can develop a more effective method to get it to the tumors, it may well have promise as an anticancer treatment," said Dr. Kurzrock. She hopes to have the liposome-encapsulated delivery system ready to test in a phase I clinical trial for patients with a variety of cancers in 2008. Whether the intravenous formulation would have more side effects in patients because of the higher blood levels of the agent is not yet known, but preliminary testing in mice has shown no toxicity, even at maximum doses.

Currently under way at M. D. Anderson is a clinical trial of curcumin in multiple myeloma, and researchers are seeking funding for a trial in breast cancer. Trials of curcumin in colorectal cancer and in myelodysplastic syndrome are in progress at other institutions. Curcumin is also in clinical trials as a treatment for non-cancer diseases such as Alzheimer's disease, arthritis, and psoriasis.

Food for thought

Dr. Aggarwal, for one, is not surprised at the evidence that curcumin may have efficacy in treating cancer. He feels curcumin has the potential to one day be an inexpensive and nontoxic alternative to harsher oncology drugs; a chemopreventive agent; and an adjunct to chemotherapy. But he notes that progress in developing curcumin for medical use is likely to be much slower than for pharmaceutical agents because curcumin can't be patented on a broad scale and therefore is unlikely to attract the interest and the funding of pharmaceutical companies.

For his part, Dr. Aggarwal takes a curcumin tablet every day, and he offers this food for thought: "The combined rate of the four most common cancers in the United States—lung, prostate, breast, and colon—is at least 10 times lower in India, where curry is a staple in the diet." ●

For more information, call Dr. Aggarwal at 713-794-1817 or Dr. Kurzrock at 713-794-1226.

In Brief

(Continued from **page 3***)*

When used as a second-line therapy in previous studies, dasatinib had a high level of activity in patients who developed resistance to imatinib, achieving a 40% response in these patients. On the basis of these findings, the researchers hypothesized that dasatinib would produce an earlier response if used first and initiated the current study to test the drug's efficacy as a first-line therapy for CML.

"In CML, earlier response correlates with a better chance of being alive and well long-term and less of a chance of developing treatment resistance," said Dr. Cortes.

CML is caused by a genetic abnormality known as the Philadelphia chromosome, which causes production of a protein that sets off a chain reaction resulting in rapid cell growth. Dasatinib (BMS-354825), a multitarget kinase inhibitor, blocks expression of the protein.

So far, 35 CML patients are enrolled in the dasatinib trial. The goal is to enroll 100 patients, follow them for a longer period, and look for other measures of molecular response.

> "In CML, earlier response correlates with a better chance of being alive and well long-term and less of a chance of developing treatment resistance."
>
> **– Dr. Cortes**

"Eventually, there will be a more direct approach, a randomized trial, to test whether dasatinib does indeed work better than standard therapy," said Dr. Cortes.

To be eligible for the current trial, patients must be age 16 years or older, have a diagnosis of CML with no or minimal prior therapy, have a good performance status, and have normal organ function. For more information, contact Dr. Cortes at 713-794-5783 or *ask*MDAnderson at 1-877-632-6789 (or visit www.mdanderson.org). ●

Unknown Cancer Origin May Be Determined Using Gene Assay

A soon-to-be commercially available gene assay can help pinpoint the tissue of origin for cancer of unknown primary site (CUP), researchers at M. D. Anderson recently demonstrated. The finding is significant because the advent of targeted therapies and management strategies focused on specific cancers makes it increasingly important to determine the molecular profiles of cancers that constitute the CUP syndrome, said Gauri Varadhachary, M.D., lead author of the study.

CUP, or metastatic disease that presents without a known primary tumor, represents 3–5% of all cancers. Exactly what makes the primary tumor disappear or stay undetectable is not well understood, and advances in imaging have not significantly increased the chances of finding the site of origin, Dr. Varadhachary said.

Using a 10-gene assay developed by Veridex, the researchers prospectively studied metastatic carcinoma tissue samples taken from CUP patients. In the ongoing study, the team found that the test predicted one of six target cancer types in 60% of the 36 patient samples. Preliminary results were presented at the 2007 meeting of the American Society of Clinical Oncology in June.

This is believed to be the first assay of its kind evaluated prospectively in only CUP patients, said Dr. Varadhachary, associate professor in the Department of Gastrointestinal Medical Oncology. It is challenging to conduct such studies to determine tissue of origin in CUP because by definition there is no primary cancer, and researchers must rely on clues from a patient's pathology, imaging data, and clinical course to indirectly validate the test results.

"Distinguishing the colon cancer profile, for example, from other disseminated CUP is of increasing significance," Dr. Varadhachary said. "The last 10 years have brought tremendous progress in the treatment of colon cancer. These regimens may have a greater impact in the colon cancer profile subset of CUP." Future studies will address whether this assay and other profiling studies affect treatment decisions and survival in CUP patients, she said. ●

Nanoparticles Deliver Tumor-Suppressor Gene

A tumor-suppressor gene has been successfully delivered into the tumors of patients with stage IV non–small cell lung cancer (NSCLC) via intravenously administered lipid nanoparticles in a phase I clinical trial at M. D. Anderson. The technique to incorporate the *FUS1* tumor-suppressor gene into DOTAP:cholesterol nanoparticles was developed at M. D. Anderson.

"We've treated 13 patients in this first-in-human study, and we've seen an exciting proof of concept with no significant drug-related toxicity," said principal investigator Charles Lu, M.D., associate professor in the Department of Thoracic/Head and Neck Medical Oncology. "The number of patients is too small to draw any definite conclusions about clinical activity, however."

A blinded analysis of pretreatment and post-treatment biopsies of three patients' tumors showed that expression of *FUS1* was absent from pretreatment samples but present at high levels after treatment. *FUS1* can induce apoptosis—programmed cell death—in cells, but the gene's expression is frequently lost when normal cells become cancerous. It is hoped that restoration of *FUS1* will shrink tumors or halt further growth.

Fever has been the only clinically significant side effect, but premedication with dexamethasone and diphenhydramine can prevent it.

The results were presented at the American Association for Cancer Research annual meeting in April.

Previous gene therapy clinical trials involved direct injection of genes into tumors. "This is the first time anyone has shown that a gene can be injected intravenously and then be taken up and expressed in cancer cells at distant sites," said Jack Roth, M.D., professor in the Department of Thoracic and Cardiovascular Surgery and a pioneer in the field of gene therapy.

Treatment of more patients is planned. For more information, call Jenny Beach, R.N., at 713-563-9156 or Jan Jenkins, R.N., at 713-563-9152. ●

HOUSE•CALL

Your First Colonoscopy: Here's What You Can Expect

Colorectal cancer is the third most common type of cancer in the United States and also one of the deadliest. Fortunately, a simple test can catch colorectal cancer before it spreads and can even help prevent it. The test is called a screening colonoscopy, and it could save your life.

"Even a modest increase in the number of colorectal cancer screenings performed would save the lives of many thousands of people annually," explained Robert Bresalier, M.D., professor in the Department of Gastroenterology, Hepatology, and Nutrition.

What is a colonoscopy?

Most colorectal cancers begin as an abnormal lump of tissue called a polyp. Polyps form on the lining of the colon or the rectum. Polyps are common—up to 20% of middle-aged and older people have one or more.

Most polyps are harmless, but some turn into cancer over time. Most people with small polyps don't have symptoms; this is why screening for colorectal cancer is so important. A colonoscopy is the most sensitive test available for finding polyps and cancer in the colon and rectum.

To perform your colonoscopy, your doctor will examine your rectum and the entire length of your colon with a long, thin, flexible tube inserted into your rectum. This instrument has a light and a lens for viewing.

During your colonoscopy, your doctor will remove any polyps he or she finds—before the polyps turn into cancer. This is one of the most effective ways to prevent colorectal cancer from forming. Also during your colonoscopy, your doctor can perform a biopsy if he or she finds anything abnormal in your colon.

Catching colorectal cancer early can save your life. Recommended screening options include:

- Screening colonoscopy every 10 years (M. D. Anderson's preferred method)
- Fecal occult blood test every year
- Flexible sigmoidoscopy every 5 years
- Annual fecal occult blood test and flexible sigmoidoscopy every 5 years (combined testing is preferred over either procedure alone)
- Double-contrast barium enema every 5 years

Screening for most people should begin at age 50, but those who are at moderate or high risk for colorectal cancer may need to begin screening earlier. More frequent exams should be performed if polyps are found.

Risk factors for colorectal cancer include family or personal history of the disease, obesity and lack of physical activity, smoking, and alcohol use. Talk to your doctor about which screening method is best for you.

Before your colonoscopy

Your doctor will give you a list of things to do to prepare for your colonoscopy. The day before your appointment, you will need to clean out your bowel by eating and drinking only clear liquids. This doesn't mean you'll be uncomfortably hungry, though, because you are allowed to have foods such as clear broth, juices, and gelatin.

Your doctor will also give you a prescription for a liquid that you will need to drink. Many patients used to find this step difficult because of the large quantity of liquid they had to drink, but the amount has decreased over the years.

One more thing you will need to do to prepare for your test is to take laxatives, which will empty your colon.

During your colonoscopy

You will be made as comfortable as possible before your colonoscopy begins. You will then be given a medication to make you relax. Many patients fall asleep and stay asleep throughout the colonoscopy. You will be carefully watched during the procedure for any signs of discomfort.

Dr. Bresalier reminds his patients that if they begin to feel discomfort, their medication can be quickly adjusted. One interesting effect of the medication commonly used is that after the procedure is over, you probably won't remember anything about it.

Occasionally, a patient feels mild discomfort after a colonoscopy. Your chances of feeling discomfort, though, are not increased if you have a polyp removed or if you have a biopsy. Complications during colonoscopies are very rare.

Communicating is key

As with any medical procedure, it's important to communicate with your doctor before and after having a colonoscopy to make sure all your questions are answered. Dr. Bresalier suggests also talking with friends or relatives who have had a colonoscopy to help clear up fears and misconceptions. ●

For more information, ask your doctor or contact M. D. Anderson's Cancer Prevention Center at 713-745-8040 or 1-800-438-6434.

To make an appointment at M. D. Anderson for a screening colonoscopy, call 713-792-4796.

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T. Locke

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DiaLog | Targeted Therapies Are Here to Stay

By Gabriel N. Hortobagyi, M.D.

At this year's annual meeting of the American Society of Clinical Oncology (ASCO), it was more apparent than ever that the paradigm of cancer treatment has irrevocably changed. In a short 15 years, targeted therapy has transformed from a dream into a substantive reality; drugs like imatinib, trastuzumab, bevacizumab, cetuximab, and others have become integral components of modern anticancer treatment.

Today, we no longer search for substances that have differential toxicity for cancer cells; instead, we identify the molecular abnormalities responsible for the malignancy and design chemical compounds or monoclonal antibodies that inhibit their activity. The current generation of trials combines these agents with chemotherapy, endocrine therapy, or other targeted therapies in the hope of inhibiting multiple signaling pathways or interfering with the dominant pathway at more than one level.

Of particular significance at this year's ASCO meeting was a report indicating that single-agent sorafenib prolonged survival of patients with advanced hepatocellular carcinoma compared to placebo and best supportive care. This is the first systemic therapy to alter the outcome of this deadly tumor.

Another study extended the indications of bevacizumab to advanced kidney cancer, showing that adding the anti-vascular endothelial growth factor (VEGF) antibody to treatment with interferon alpha A2 nearly doubled progression-free survival, from 5.4 to 10.2 months. Thus, after decades of assessing mostly ineffective treatments for renal cell carcinoma, we now have four highly effective targeted therapies for use in the disease: sorafenib, bevacizumab, tensirolimus, and sunitinib. Now studies will seek to determine optimal combinations of these and other agents in managing this tumor.

Another highly refractory tumor, advanced thyroid cancer, also yielded ground to a molecularly targeted therapy. Axitinib, a VEGF inhibitor, was reported to produce major responses in 22% of patients with advanced thyroid cancer and disease stability in another 50%. This is the first systemic agent to show antitumor efficacy in this tumor type.

I feel confident that as these strategies evolve, most types of cancer will become increasingly treatable, more frequently curable, and sometimes even preventable. We must, however, increase participation in clinical trials if we are to accelerate the pace of progress. I urge physicians to educate their patients about opportunities to receive novel therapies and encourage them to seek out clinical trials when appropriate. ●

Dr. Hortobagyi is chair of and professor in M. D. Anderson's Department of Breast Medical Oncology and immediate past president of the American Society of Clinical Oncology.

OncoLog, M. D. Anderson Cancer Center's report to physicians, is a monthly newsletter sent to more than 30,000 physicians throughout the nation and the world. Published by the Department of Scientific Publications, *OncoLog* reports on innovative developments in research and treatment at M. D. Anderson. Current and previous issues are available online in English and Spanish at www2.mdanderson.org/depts/oncolog. For editorial information, call 713-792-3305 or email scientific publications@mdanderson.org. To refer a patient or request information, call 1-877-632-6789 or 713-792-6161, or visit www.mdanderson.org.

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