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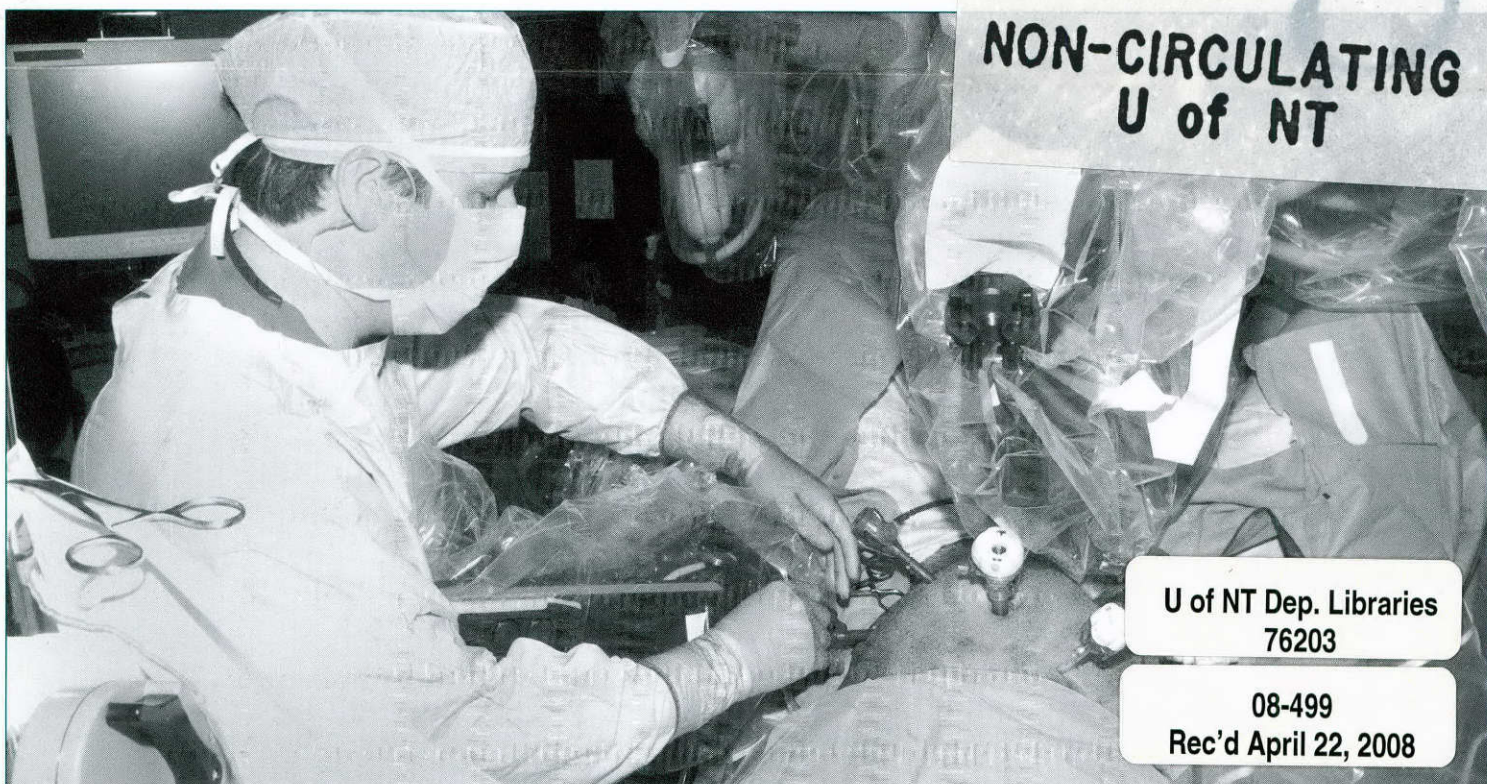


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REPORT TO PHYSICIANS

JANUARY 2008 VOL. 53, NO. 1

# Oncology



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Dr. John W. Davis adjusts the laparoscopic arms during a robot-assisted prostatectomy in M. D. Anderson's robotic surgery suite.

## Prostate Cancer: A Tale of Two Therapies

Robot-assisted surgery and active surveillance give patients with localized prostate cancer a chance at surviving the disease with fewer complications.

By John LeBas

Prostate cancer is a tricky foe. On the plus side, long-term overall survival is very high when the disease is found and treated before metastasis. But on the negative side, treatment may result in such side effects as decreased sexual, bladder, and bowel functions.

Fortunately, two very different treatment options have emerged: robot-assisted radical prostatectomy, which may cure the disease while avoiding side effects, and active surveillance, which keeps patients off treatment unless regular testing detects disease progression. Physicians at The University of Texas M. D. Anderson Cancer Center say such treatment

(Continued on page 2)

THE UNIVERSITY OF TEXAS  
MD ANDERSON  
CANCER CENTER

## Prostate Cancer: A Tale of Two Therapies

(Continued from page 1)

options are allowing them to eradicate or control prostate cancer in more men with less reduction in their quality of life.

### Robotic surgery: Precision is key

In M. D. Anderson's robotic surgery suite, a patient lies belly-up on the operating table. A 1,500-pound robotic machine hulks overhead, its four metallic arms inserted into the man's abdomen. Yet for all its bulk, this surgeon-controlled device is performing the most delicate of tasks—removal of a cancerous prostate, a procedure in which a successful outcome is determined in millimeters.

At the helm is Dr. John W. Davis, an assistant professor in M. D. Anderson's Department of Urology. From a nearby console that looks like an arcade racing game, he controls the robot's movements using toggles and pedals while watching a 3-D video feed from a camera inside the patient.

His other tools are essentially the same as any other surgeon's—gripping, snipping, and cauterizing instruments. But the advantage is that they, too, are attached to the robot's laparoscopic arms, which allow Dr. Davis to access and remove the diseased prostate with minimal tissue disturbance and a high degree of precision. "The point," he says, "is that this is minimally invasive."

Impotence and urinary incontinence have long been among the possible complications resulting from radical prostatectomy. But in robot-assisted surgery, which is essentially next-generation laparoscopic surgery, the surgeon has the opportunity to reduce such complications. The reasons for this become clear as the procedure plays out on one of the video monitors in the surgical suite.

The laparoscopic arms, which taper down to less than a half an inch in diameter, are inserted through a row of four evenly spaced incisions across the patient's abdomen. As is true in other laparoscopic surgeries, this reduces the amount of muscle and other tissue that must be cut, reducing the time needed to heal. Most patients who undergo a robot-assisted prostatectomy are walking within a day.

Once the arms are inside the patient, Dr. Davis can see most of the pelvic

cavity and position the tools as needed. He separates connective tissue to move the arms past the bladder; the robotic device allows him to make precise cuts and avoid damaging nerves that control erectile function. Bleeders are quickly sealed with the cauterizing tool, if appropriate. However, near the nerve bundles that control erectile function, bleeders are carefully clipped or oversewn to avoid thermal damage. "Having a magnified, 3-D view and reduced bleeding is a tremendous advantage. The biggest challenge of open surgery is the smaller field of view," says Dr. Davis, who has performed more than 400 robot-assisted radical prostatectomies.

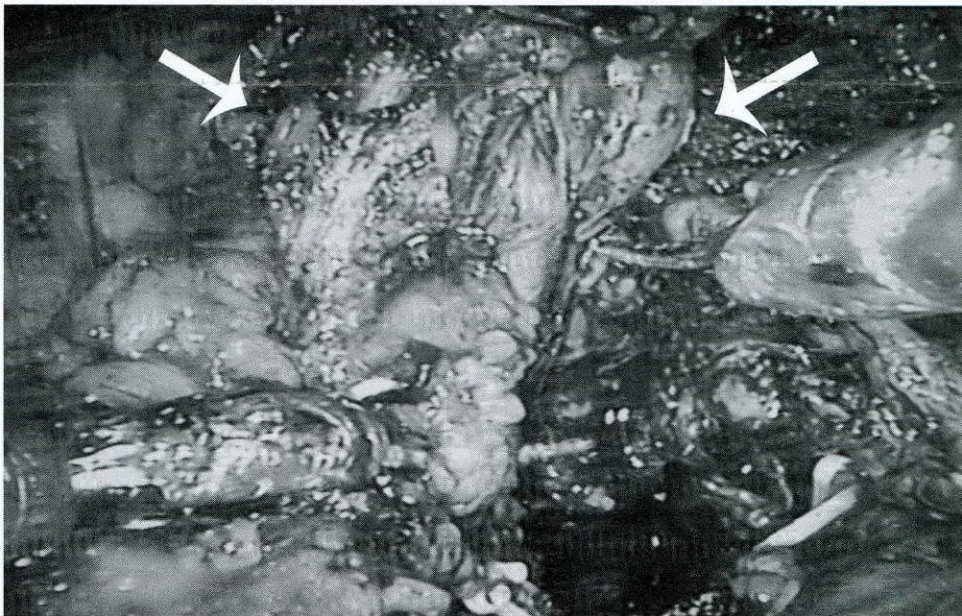
Then, the diseased prostate is revealed as he snips through the bladder. He carefully slices the prostate free—and precision here is key, since clear surgical margins are desired but there is little tissue to spare. "The prostate is surrounded by so much, such as nerves, the rectum, and urinary control muscles," Dr. Davis says. "Treating prostate cancer with surgery is a different game than surgery for colon cancer, for example. We don't have 5 extra centimeters to work with—the margins are measured in millimeters." Once resected, the prostate is dropped into a small plastic bag and extracted through one of the laparoscopic tubes.

But the surgery isn't over yet. Dr. Davis must also remove lymph nodes so they can be examined for signs the cancer has spread. The robot allows him to strip these tiny sacks away from the large pelvic blood vessels and nerves that go to the legs. Lastly, to prevent urinary incontinence, he reconstructs the bladder-urethra connection—severed during the prostate removal—using a needle and suture passed down through a laparoscopic arm. In this two-layer reconstruction, a few stitches are placed to connect the urethra and bladder, which will drain through an artificial catheter until normal urinary function can resume. A single supportive stitch placed at the pelvic wall will hold the bladder in proper position and enhance muscular control. Suturing must be precise to avoid damage to the urinary control muscles.

With that, the laparoscopic arms are removed, the robot is wheeled away, and the patient's incisions are sutured—leaving relatively little outside evidence of major surgery.

### Deciding how—and when—to treat

Radical prostatectomy is frequently recommended for the treatment of localized prostate cancer because it can usually eradicate the disease. The younger a man is when prostate cancer



Video feed shown on a monitor in the robotic surgery suite provides an up-close view of a cancerous prostate (indicated by the arrows).

is diagnosed, the more likely he is to be referred for a radical prostatectomy. The median age of men who undergo prostate surgery is about 62 years, with a range of about 40 to 70 years. Depending on the patient's age and health status, other options for treating prostate cancer may include forms of radiation therapy, such as proton therapy and brachytherapy—all of which carry their own set of side effects.

Prostate cancer often progresses slowly, and since the introduction of prostate-specific antigen (PSA) testing about 20 years ago, early detection has risen sharply. Accordingly, questions have arisen about whether a prostatectomy should be performed in men who may be more likely to die of other causes.

"Because of widely available PSA screening, a lot of men are diagnosed with low-grade, very small prostate cancers, but there is no evidence that earlier detection of this type of disease means longer survival," said Dr. Jeri Kim, an associate professor in Genitourinary Medical Oncology. "Because of the sensitivity of the PSA test, clinically insignificant tumors sometimes are diagnosed and patients may, as a consequence, be overtreated with radiation or surgery. If we can avoid unnecessary treatment and its side effects in these men, that would be a major quality-of-life advancement."

Dr. Kim is principal investigator of a trial that is testing "active surveillance" for prostate cancer to help clinicians determine which men belong in that category. Active surveillance takes the older concept of "watchful waiting" a step further. Rather than waiting for clinical signs of metastatic disease—when it is too late to eradicate prostate cancer—the researchers are using a regular testing regimen that closely and frequently monitors patients for disease progression. No treatment is started unless certain progression triggers are observed.

A major goal of the study is to reliably identify patients who can forgo treatment, preventing unnecessary interventions and, thus, unnecessary complications, Dr. Kim said. But the investigators also hope their study of patients' tissue



**If we can avoid unnecessary treatment and its side effects in these men, that would be a major quality-of-life advancement."**

— Dr. Jeri Kim

and blood specimens will yield molecular markers for prostate cancer. In the end, they also want an improved risk model to emerge, one that better predicts how and why tumors progress.

"Right now, treatment recommendations are based largely on PSA levels and Gleason scores," Dr. Kim said. A Gleason score is a disease assessment based on microscopic evaluation of cancerous prostate tissue. "That has served us well, but not all patients with the same cancer profile have the same progression rate. By incorporating molecular markers and redefining low-risk patients, we can develop risk-adaptive management for early prostate cancer."

The trial, which opened in February 2006, aims to accrue 650 patients. It has three study arms: patients with low-risk disease; those with localized disease who have chosen not to receive treatment; and those who have co-morbidities and thus are not candidates for surgery or radiation therapy. New participants are still being accepted.

In the study, a PSA test and physical exam are conducted every 6 months, and transrectal ultrasonography is performed annually. A core biopsy is performed upon entry to the study and again after 1 year; the frequency of later biopsies may vary depending on the

outcome of the initial set of biopsies. The patients are surveyed twice a year about their quality of life and dietary habits. Additionally, a support group led by staff psychologists meets monthly to help patients deal with the anxiety that often results from not actively engaging in treatment and to provide information about prostate cancer.

Any of the following would trigger a recommendation to begin treatment: indication of cancer on repeat biopsy, upgrade of the patient's Gleason score, an increase in tumor size, and a 30% increase in PSA level from the baseline level. The investigators have found that most patients do not meet the disease progression benchmarks during the first year of active surveillance.

### Looking ahead

No long-term clinical data have been published on how robot-assisted surgery and active surveillance are improving patients' quality of life, but the fact is that fewer damaging and unnecessary treatments are being done, Dr. Davis said. M. D. Anderson recently invested in a second surgical robot, one that will offer even better range of motion and will double the institution's capacity for ever-more-popular robotic procedures. And the techniques are being refined, through such methods as a protocol designed by Dr. Davis that separates organ and lymph node dissection between two surgeons to see if this improves cancer control.

Meanwhile, research into alternative methods of treating prostate cancer continues. For example, an upcoming cryotherapy protocol for patients with early prostate cancer will attempt to control the disease by freezing part of the prostate.

"Compared to 10 or 20 years ago, we can offer prostate cancer patients a greater chance at recovery while minimizing quality-of-life complications," Dr. Davis said, "and we will have even better therapy options in the future." ●

For more information, call Dr. Davis at 713-792-3250, Dr. Kim at 713-792-2830, or M. D. Anderson's patient referral line at 1-877-632-6789.

# Making Headway Against Myeloproliferative Disorders

For years, progress against this family of rare blood disorders was stagnant, but the recent discovery of a key genetic mutation has launched a flurry of promising treatments.

By Don Norwood

Until very recently, patients with myeloproliferative disorders—hematological diseases in which the blood-producing cells in the bone marrow undergo abnormal development and malfunction—faced an uphill battle in their treatment because of the relative rarity of these disorders.

As for other rare diseases, pharmaceutical companies have been hesitant to develop drugs for myeloproliferative disorders. Thus, even though these disorders cause myriad health problems and in some cases lead to acute leukemia, little headway had been made in finding effective therapies—that is, until a recent discovery. This discovery of a key gene mutation has led to the development of new drugs that appear to control myeloproliferative disorders and their symptoms, giving new hope to patients who suffer the diseases' debilitating effects.

The three main myeloproliferative disorders are polycythemia vera, essential thrombocythemia, and primary myelofibrosis. Patients often experience such symptoms as headache, fatigue, shortness of breath, easy bruising or bleeding, petechiae, unexplained weight loss, night sweats, and fever. The symptoms unique to the different disorders are no less debilitating. In those with polycythemia vera, overproduction of red blood cells can lead to swelling of the spleen; patients may also have

widespread itching. For patients with essential thrombocythemia, excess platelet production can make the blood “sticky,” slowing blood flow. Patients with primary myelofibrosis develop scarring or thickening of the fibers in the bone marrow, leading to decreased red blood cell production, anemia, and low numbers of platelets and white blood cells; the spleen subsequently enlarges as it takes over the production of blood cells from the bone marrow.

## Low incidence, big breakthrough

Because of the rarity of myeloproliferative disorders, most organizations that track disease incidence do not track these disorders. According to 2001-2004 Surveillance, Epidemiology and End Results data, the combined annual incidence of myeloproliferative disorders in the United States was 2.1 per 100,000 individuals. In comparison, the mean annual incidence of prostate, breast, lung, and colorectal cancers during that period was 172 per 100,000 men, 130 per 100,000 women, 63 per 100,000 population, and 51 per 100,000 population, respectively.

The progression of and prognosis for myeloproliferative disorders vary greatly, as some patients must undergo only close monitoring of their disease, whereas others have rapid progression to advanced-stage disease or even to acute myelogenous leukemia. Furthermore, myeloproliferative disorders can develop at any age, and researchers have yet to identify causes for them. Even with treatment, these disorders can be fatal.

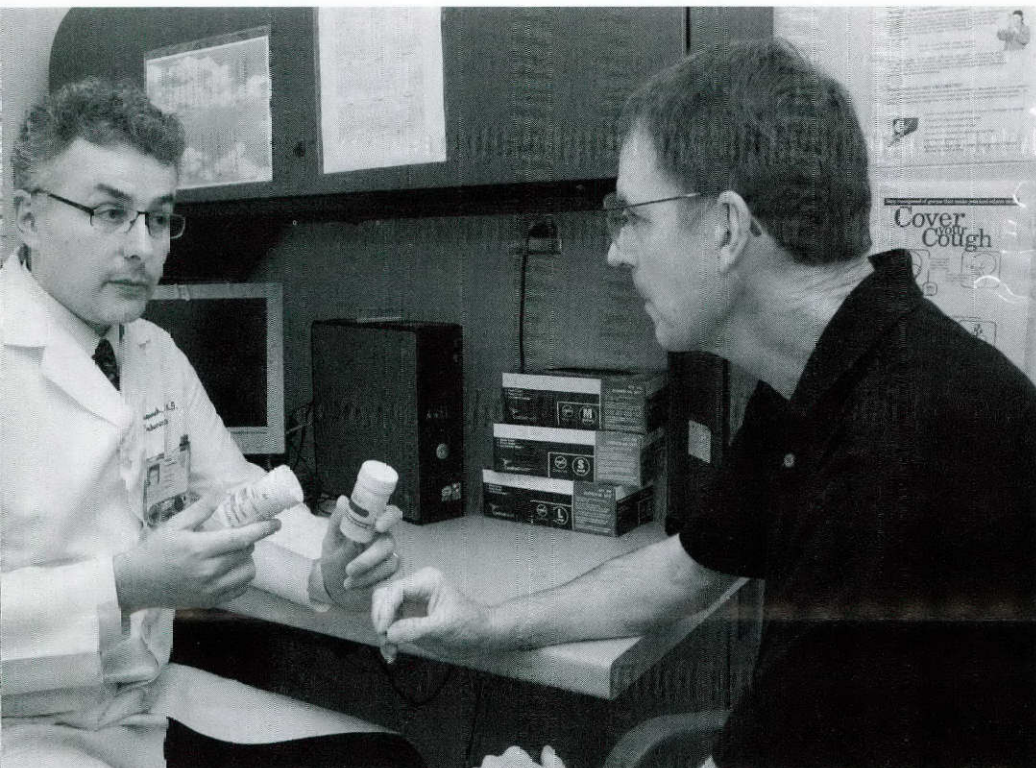
The discovery that prompted pharmaceutical and biotechnology companies to develop more effective therapies occurred in 2005, when researchers found a mutation of the *JAK2* gene in

very large percentages of patients with the three main myeloproliferative disorders. While exact causes of the disorders remain unknown, the discovery of the mutation resulted in the development of *JAK2* inhibitors, and this has paid significant dividends for patients.

Initially discovered by a group of researchers in France, the *JAK2* gene is mutated in more than 90% of patients with polycythemia vera and about 50% each of patients with essential thrombocythemia and primary myelofibrosis. Physiologically, the *JAK2* protein, a tyrosine kinase, plays an important role in cell growth. In patients with the mutation in the *JAK2* gene, the *JAK2* protein is autophosphorylated, meaning that it is always active, resulting in the overproduction of blood cells, said Srdan Verstovsek, M.D., Ph.D., associate professor in the Department of Leukemia at M. D. Anderson. “The *JAK2* protein helps transfer signals from growth factors that usually circulate in the blood and attach to the growth factor receptors on the cell surfaces,” Dr. Verstovsek said. The receptors activate *JAK2*, which then carries signals through a cascade of proteins to the cell nuclei. This tells the cells to grow.

About half of patients with essential thrombocythemia or primary myelofibrosis do not have the *JAK2* mutation. However, researchers have found that a small percentage of these patients have other mutations and that the *JAK2* inhibitors may also be beneficial for them, said Dr. Verstovsek.





*Dr. Srdan Verstovsek discusses the results of therapy with patient Lee Willis, who is being treated with a new drug for myelofibrosis. Mr. Willis's disease showed a dramatic response within 1 month, with the reduction of an enlarged spleen and other symptoms that result from this myeloproliferative disorder.*

### **New hope for control**

In the short period since the discovery of the JAK2 mutation, development and clinical testing of several agents that inhibit JAK2 have occurred. These agents include INCB18424, XL019, and CEP701, which are currently being evaluated in clinical studies for patients with advanced primary myelofibrosis.

M. D. Anderson has been at the forefront of clinical testing of JAK2 inhibitors for the treatment of myeloproliferative disorders, said Charles A. Koller, M.D., medical director of the Leukemia Center and professor in the Department of Leukemia. Currently, Dr. Verstovsek is conducting several clinical trials of JAK2 inhibitors for myeloproliferative disorders. Furthermore, the number of patients with myeloproliferative disorders seeking participation in clinical trials at M. D. Anderson has greatly increased, from 34 in 2003 to 214 in 2006.

"We realized the potential for developing medications for this particular abnormality and helped design and elicit approval of these studies through the U.S. Food and Drug Administration," said Dr. Verstovsek. "So the studies were offered to patients rather quickly." Dr. Koller emphasized this quick drug devel-

opment by pointing out that the period from discovery of the JAK2 mutation to the first human trial of a JAK2 inhibitor was only about 2.5 years. This is significantly shorter than the typical time required to develop therapies in response to scientific discoveries.

Thus far, the JAK2 inhibitors that are being tested appear to be improving the quality of life of patients with myeloproliferative disorders, which is no small feat. Consider patients with primary myelofibrosis who suffer from an enlarged spleen. An enlarged spleen can intrude upon the space that the stomach normally takes up, said Dr. Koller. As a result, when the patient eats, he or she becomes full before sufficient amounts of food are eaten, resulting in weight loss. Before the development of JAK2 inhibitors, the only way to relieve an enlarged spleen in such patients was to perform a splenectomy. Now, however, JAK2 inhibitors can regulate the number of blood cells that pass through the spleen, preventing buildup of the cells in the spleen and the swelling that results. Researchers have observed significant and rapid decreases in the size of the spleen and the number of circulating white blood cells; this has led to

the reduction or elimination of many other symptoms, including shortness of breath, fatigue, weakness, itching, bone pain, early satiety, and weight loss. The end result has been much improved energy level and performance status.

"We know that by inhibiting JAK2, we can get rid of the manifestations of myeloproliferative disorders," said Dr. Koller. "I'm convinced that the JAK2 inhibitors will be key to controlling these diseases. I think that's going to have a significant impact on the quality of life for these patients."

The only drawback of these drugs is that they interrupt normal JAK2 function, which in turn interrupts normal cell growth. However, Dr. Koller believes that within the next 5 years, researchers will develop agents that do not have this negative effect.

### **Patient involvement driving advances**

Dr. Verstovsek confirmed that the early results of the studies of JAK2 inhibitors are very positive. "Our preliminary results already show that these medications have the potential to affect the patients in a positive way in a rather short period of time," he said. "Furthermore, many patients come to M. D. Anderson knowing about the potential of these medications, and thus they try to enroll in specific studies if they are eligible."

Key ingredients in letting patients with myeloproliferative disorders know about such trials are patient advocacy groups such as the CMPD Education Foundation, an organization that Dr. Verstovsek knows well, as he serves on its six-person medical advisory board. The foundation publishes a Web site ([www.mpdinfo.org](http://www.mpdinfo.org)) and a newsletter with information for patients with myeloproliferative disorders. This foundation, along with the MPD Foundation ([www.mpdfoundation.org](http://www.mpdfoundation.org)), is an important avenue for patients to learn about clinical trials.

Because of the rarity of myeloproliferative disorders, patients are not likely to encounter others with these diseases in their daily lives. However, through the efforts of the foundations and communication through M. D. Anderson's Department of Leukemia Web site, patients with myeloproliferative disor-

*(Continued on page 6)*

## Making Headway Against Myeloproliferative Disorders

(Continued from page 5)

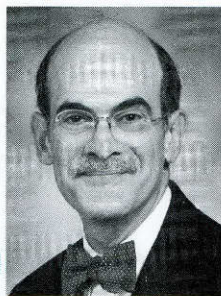
ders can learn about clinical trials offering new hope.

“We’ve been in contact with patients with myeloproliferative disorders for a decade,” said Dr. Koller. “That’s why there’s no shortage of patients. They’ve figured out that JAK2 is the key here and they want to get it inhibited.”

As the research in this field develops, the close relationship between the Department of Leukemia and these patient groups may pay even bigger dividends.

### A clearer picture emerging

An additional achievement that has benefited patients with myeloproliferative disorders is the improved classification of these diseases. To help make diagnosis of myeloproliferative disorders more precise, M. D. Anderson has worked with other institutions to both update and streamline the diagnostic criteria for the diseases. Among the changes: a patient’s JAK2 mutation status is now determined as part of the diagnostic process. This determination, which can be accomplished with a simple blood test, helps significantly in making a proper diagnosis—previously, no single test could effectively differentiate between the myeloproliferative disorders and other similar bone marrow diseases, Dr. Verstovsek said. The results of this collaboration will be pub-



**“I’m convinced that the JAK2 inhibitors will be key to controlling these diseases.”**

— Dr. Charles A. Koller

lished in the next edition of the World Health Organization’s “blue book” for hematological neoplasms (*World Health Organization Classification of Tumours: Pathology and Genetics: Tumours of Haematopoietic and Lymphoid Tissues*).

In addition, M. D. Anderson has organized and taken part in three meetings of the International Working Group for Myelofibrosis Research and Treatment. These were designed to help myelofibrosis experts come to a consensus regarding different issues in the treatment of the disorder. As a result, the experts decided on a set of clinical response criteria that should be

used in clinical studies of myelofibrosis. These criteria were published in 2006 and are now in use across the board in clinical trials.

Also recently published as a result of these meetings is a definition of the transformation of essential thrombocythemia and polycythemia vera to myelofibrosis, a phenomenon that occurs in 25% of patients; these findings also will be published in the World Health Organization’s hematological neoplasms blue book. The transformation is important because myelofibrosis is associated with a much shorter life expectancy (5–7 years) than essential thrombocythemia and polycythemia vera (20 years or more).

“These are the issues that have troubled this community for a long time,” said Dr. Verstovsek. “Now, with the new findings and with the common effort from all sides to streamline procedures for diagnosis, for therapy, for definition, and so forth, the field is becoming clearer and physician-friendly so that we can enroll patients in studies and administer potentially effective therapies for myeloproliferative disorders in a uniform fashion.” ●

For more information, visit the Department of Leukemia’s myeloproliferative disorders Web site at [www.mdanderson.org/diseases/mpd](http://www.mdanderson.org/diseases/mpd).

## Clinical Trials in Myeloproliferative Disorders

- A Phase II Study: 2-Chlorodeoxyadenosine and Cytarabine in Idiopathic Hypereosinophilic Syndrome (DM97-232). Principal Investigator (PI): Michael Andreeff, M.D., Ph.D. This clinical research study will look at whether 2-chlorodeoxyadenosine (2-CdA) plus cytarabine helps patients with idiopathic hypereosinophilic syndrome. In this syndrome, the number of white blood cells (eosinophils) is greatly increased, and these cells invade the heart, brain, liver, and lungs.
- A Prospective Open-Label Pilot Trial of PS-341 (Bortezomib) in Symptomatic Advanced Myeloproliferative Disorders (2005-0284). PI: Srdan

Verstovsek, M.D., Ph.D. The goal of this Phase II clinical research study is to learn if bortezomib can help control disease in patients with symptomatic, advanced myeloproliferative disorders. The safety of bortezomib in patients with myeloproliferative disorders will also be studied.

- A Phase II Study of CC-4047 in Myelofibrosis with Myeloid Metaplasia (2006-0817). PI: Srdan Verstovsek, M.D., Ph.D. This clinical research study is comparing treatment with CC-4047 to treatment with a combination of CC-4047 and prednisone. The goal is to find a treatment regimen so further study can

be done in patients with myelofibrosis with myeloid metaplasia. The safety of these treatments is also being studied.

- A Phase I/II, Open-Label Study of the JAK2 Inhibitor INCB018424 in Primary Myelofibrosis and Post Polycythemia Vera/Essential Thrombocythemia Myelofibrosis (2007-0169). PI: Srdan Verstovsek, M.D., Ph.D. The goal of this clinical research study is to find the highest tolerable dose of INCB018424 that can be given to patients with myelofibrosis. Another goal is to see if the drug can help control disease. The safety of this drug will also be studied. ●



## What You Should Know About Male Cancers

**M**any men are uncomfortable discussing their genitals and prostate, even at the cost of their own well-being. But for cancers that happen only in men, watching for symptoms and talking to your doctor can mean the difference between life and death.

### Prostate cancer

One man in 6 will be diagnosed with prostate cancer during his lifetime. Although prostate cancer is the second-leading cause of cancer-related death among men in the United States, the chance of surviving prostate cancer is nearly 100% if it is found early.

You are more likely to get prostate cancer as you get older, especially after age 50 years. African-American men and men with a family history of prostate cancer have a higher risk of developing the disease.

Finding prostate cancer early can be difficult because it usually doesn't have any symptoms. That's why it is important to see your doctor for regular examination and testing. However, any of the following symptoms may be a sign of prostate disease:

- Frequent urination
- Painful or burning sensation during urination
- Difficulty starting or stopping urine flow
- Weak or interrupted urine flow
- Persistent pain or stiffness in your lower back, hips, or upper thighs

M. D. Anderson recommends that beginning at age 50—or at age 45 for African-American men and men with a family history of prostate cancer—men be screened every year for prostate cancer. Prostate cancer screening is done with a digital rectum exam, a prostate-specific antigen test, or both. During a digital rectum exam, the doctor inserts a gloved, lubricated finger into the rectum and feels the prostate

for lumps, enlargement, or anything else that seems unusual. A prostate-specific antigen test is a simple blood test that can help a doctor decide if further action is needed. It is always a good idea to talk to your doctor about the risks, benefits, and limitations of prostate cancer screening.

### Testicular cancer

Only about 1 in 300 men will develop testicular cancer during his lifetime. Testicular cancer is the most common cancer in men between the ages of 20 and 34 years. Although there is no formal screening for it, testicular cancer may be discovered during a routine physical examination. The best way to detect testicular cancer early is to know what is “normal” for your testicles. Look at and feel your testicles at least once a month, and see your doctor if you experience any of the following for more than 2 weeks:

- A small, hard, often painless lump on a testicle
- A feeling of heaviness in the scrotum
- A dull ache in the lower abdomen or groin
- A sudden collection of fluid in the scrotum
- Pain or discomfort in a testicle or in the scrotum

Men with a family history of testicular cancer have a higher risk of developing the disease, and those who have already had cancer in one testicle are more likely to get it in the other testicle. White men are 5 to 10 times more likely to develop testicular cancer than men of any other race. Men with undescended testicles—even if surgery was done to correct this—are also at a higher risk, and so are men whose testicles did not develop normally and men who have Klinefelter's syndrome (a disorder that causes low levels of male hormones).

### Penile cancer

Cancer of the penis is very rare; it affects only about 1 in 100,000 men each year in the United States. Penile



**One man in 6 will be diagnosed with prostate cancer during his lifetime.**

cancer is most common in men ages 50 to 70 years. Symptoms of penile cancer may include:

- A rash-like redness on the penis
- A lump on the penis
- A wart-like growth or lesion on the penis
- An open sore on the penis that does not heal

These symptoms may not mean that you have penile cancer, but you should still see a doctor about them as soon as possible. There is no formal screening for penile cancer.

Men who were not circumcised at birth may be at a greater risk of developing penile cancer. Human papillomavirus (HPV) infection may increase the risk of developing penile cancer. Other risk factors for penile cancer include having phimosis (a condition in which the foreskin of the penis is difficult to pull back from the head), having poor genital hygiene, having many sexual partners, and using tobacco products. ●

*For more information, talk to your physician, or:*

- call askMDAnderson at 1-877-632-6789
- visit [www.mdanderson.org](http://www.mdanderson.org)
- visit the National Cancer Institute online at [www.cancer.gov](http://www.cancer.gov) or the American Cancer Society online at [www.cancer.org](http://www.cancer.org).

**Oncolog, January 2008**  
J. Munch

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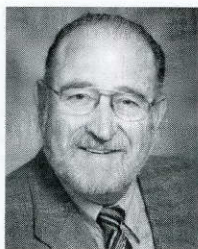
## IN BRIEF

### Newly Identified Gene May Stop Development of Lung Cancers

Researchers at M. D. Anderson have identified a new tumor-suppressor gene for lung cancer in mice, and their findings suggest the gene, *GPRC5A*, may suppress lung cancer development in humans as well. The findings were reported in the Nov. 21, 2007, edition of the *Journal of the National Cancer Institute*.

Reuben Lotan, Ph.D., professor in the Department of Thoracic/Head and Neck Medical Oncology, and colleagues previously demonstrated that the *GPRC5A* transcript is detected in healthy lung tissue more frequently than in other tissue but that it is underexpressed in non-small cell lung cancer and in head and neck squamous cell carcinomas in humans. These findings suggest that, when present, the gene plays a role in suppressing the development of cancer.

The recent study found that, in mice, deletion of the *GPRC5A* gene was associated with the development of more precancerous lung lesions and with a more frequent progression of these lesions to malignancy. In mice without the *GPRC5A* gene, lung adenomas developed during the second year of life in 76%, and adenocarcinomas developed in 17%. In comparison, only 10% of mice with the activated gene



**“To our knowledge, this is the first mouse model in which the deletion of a single gene expressed in the lungs leads to lung cancer development.”**

**– Dr. Reuben Lotan**

developed adenomas, and none in this group developed lung cancer.

“To our knowledge, this is the first mouse model in which the deletion of a single gene expressed in the lungs leads to lung cancer development,” said Dr. Lotan. “We think the findings may extend to human lung cancers as well, based on our comparative analysis of paired human normal and malignant lung tissues.”

In addition, the researchers inserted the *GPRC5A* gene into human lung cancer cell lines in the laboratory and found that the gene suppressed formation of cancer cell colonies by 91%. “Further study substantiating the gene’s role in humans could lead to the development of new approaches to prevention, diagnosis, and treatment of lung cancer,” Dr. Lotan said. ●

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