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PROSTATE CANCER
EDUCATION & SUPPORT

HOTSHEET

March 2009

MEDICARE WIDENS DRUGS IT ACCEPTS FOR CANCER

Medicare, with little public debate, has expanded its coverage of drugs for cancer treatments not approved by the FDA. Cancer doctors had clamored for the changes, saying that some of these treatments, known as off-label uses, were essential if patients were to receive the most up-to-date care. But for many such uses there is scant clinical evidence that the drugs are effective, despite costing as much as \$10,000 a month. Because the drugs may represent a patient’s last hope, though, doctors are often willing to try them.

The new Medicare rules are the latest twist in a protracted debate over federal spending on off-label drugs – those prescribed for uses other than what they were specifically approved. Proponents of the changes say such spending not only helps patients, but can also enhance medical understanding of which treatments work against various forms of cancer. But opponents argue that the new approach may waste money and needlessly expose patients to the side effects of drugs that may not help them. They also raise the possibility of conflicts of interest, because the rules rely on reference guides that in some cases are linked to drug makers.

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EXPERTS URGE PROSTATE CANCER ‘MAN-O-GRAM’

Prostate cancer experts have urged the US Congress and the incoming Obama administration to make a major research commitment to find better detection methods, including what they call a “man-o-gram.” Their idea involves a sophisticated ultrasound, magnetic resonance imaging or other method to find dangerous prostate tumors, akin to the common mammogram scans used to find breast tumors.

Dr. Faina Shtern, who heads the Boston-based nonprofit AdMeTech Foundation coordinating the advocacy effort, said \$500 million in research funding is needed over five years.

Many men now have a blood test measuring levels of a protein produced by the prostate gland called prostate-specific antigen, or PSA. Elevated PSA levels may indicate prostate cancer, but benign conditions can also raise levels. Men with elevated PSA often must have an invasive biopsy to test prostate tissue for cancer. Only about 25 percent to 30 percent of men who have the biopsy actually turn out to have prostate cancer. And experts believe that many cancers detected after PSA screening are so minor they would never present a threat if left untreated.

There is a controversy among cancer

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PROSTATE CANCER MAY CAUSE NEGLECT OF OTHER ILLNESSES

The majority of men with early-stage, low- or moderate-grade prostate cancer die from causes other than prostate cancer, researchers report in the January 2009 issue of the *Journal of the American Geriatric Society*. Therefore, prevention and management of other health conditions is important in these patients.

“Once a diagnosis of cancer has been made, it can become the sole focus of medical care,” Dr. James S. Goodwin and colleagues write. “This is understandable, because cancer is typically life threatening and often requires dramatic therapy. But earlier cancer diagnoses, due to screening, and improvements in treatment have been associated with lower cancer mortality,” they note. “Thus, patients are living longer after a diagnosis of cancer,” where other illness may have a substantial effect on their survival, they point out.

Goodwin, of the University of Texas Medical Branch, Galveston, and colleagues used data from the Surveillance, Epidemiology, and End Results (SEER) Medicare database to assess the outcome of 208,601 men between the ages of 65 and 84 years diagnosed

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THALIDOMIDE FOR THE TREATMENT OF BIOCHEMICALLY RECURRENT PROSTATE CANCER

Thalidomide may have use in the treatment of men who have biochemical recurrence of prostate cancer or a rise in their prostate-specific antigen (PSA) count after definitive therapy, according to a new randomized study from the National Cancer Institute published online 23 January 2009 in the *Journal of Urology* (Vol. 181, pp.1104-13).

In this population, the use of thalidomide was associated with an increase in PSA progression-free survival after intermittent androgen-deprivation therapy (ADT). The median time to a new PSA increase was 17.1 months for thalidomide (vs 6.6 months for placebo) in the second phase of the study's crossover design. The effect occurred despite the fact that thalidomide, which has antiangiogenic activity, had no effect on testosterone, note the study authors, led by William D. Figg, PharmD, head of the Molecular Pharmacology Section of the Center for Cancer Research at the National Cancer Institute, in Bethesda, MD.

However, the use of ADT against "biochemical recurrence" was questioned in an accompanying editorial comment. "PSA relapse after definitive therapy is common and is often associated with an excellent prognosis," writes Tomasz M. Beer, MD, associate professor of medicine in the Division of Hematology and Medical Oncology at the Oregon Health and Science University Cancer Institute, in Portland, OR. "Hormonal therapy has not been shown to improve overall survival or delay clinically meaningful events in this setting."

But the researchers point out that intermittent ADT is "increasingly being used in patients with biochemical recurrence," and there might be "a role for instituting early treatment," they suggest. In outlining their rationale for the study, the authors further explain that there is some research that suggests that ADT is better sooner rather than later. "The increasing use of ADT is based on studies suggesting clinical benefit in patients with early-stage prostate cancer treated earlier with ADT compared to those receiving it

later in the disease course."

Dr. Figg and colleagues also note that the efficacy of antiangiogenic agents, such as thalidomide, is likely to be the greatest early on, when the disease burden is minimal. The drug was previously shown to be effective in combination with chemotherapy against metastatic prostate cancer (*Clinical Cancer Research* Vol. 7, p. 1888, 2001 and the *Journal of Clinical Oncology* 2004; Vol. 22, pp. 2532, 2004) and, thus, was a candidate for treatment in earlier-stage disease, they suggest.

All patients in the study had androgen-dependent adenocarcinoma of the prostate and 2 consecutively increasing PSA counts after local definitive therapy with radical prostatectomy, radiation therapy, or cryosurgery. In phase A of the analysis, 147 patients were initially administered gonadotropin-releasing hormone agonists (GnRH-A) for 6 months, and subsequently received thalidomide or placebo. GnRH-A generally consisted of leuprolide (22.5 mg every 3 months) or goserelin (10.8 mg every 3 months). For patients in phase A, the median time to PSA progression for those taking thalidomide was 15 months, compared with 9.6 months for those taking placebo (P = 0.21).

Once patients had PSA progression, defined by an increasing PSA greater than 5 ng/mL or reaching a minimum of 1 ng/mL, they were retreated with a GnRH-A for another 6 months, and then crossed over to the opposite treatment. This was phase B, which was completed by 88 patients. The median time to PSA progression during phase B for the thalidomide group was 17.1 months, and for the placebo group was 6.6 months (P = 0.0002).

Thalidomide had no grade 3 or 4 toxicities that occurred in more than 5% of patients. Grade 2 hot flashes occurred in nearly half of the men in both the thalidomide and placebo groups, likely because of the ADT. The second most common side effect was grade 2 constipation, occurring in 41% of drug-treated men and in 16% of placebo-

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MEDICARE WIDENS DRUGS IT ACCEPTS FOR CANCER

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The new policy, which took effect in November, makes it much easier to get even questionable treatments paid for, critics of the changes say. Medicare is providing “carte blanche in treatment for cancers,” said Steven Findlay, a health policy analyst for Consumers Union. He said overly expansive coverage encourages doctors to use patients as guinea pigs for unproved therapies. It is unclear how much precedent Medicare’s new rules might have on private insurers, which often follow the agency’s lead on paying for drugs.

Medicare officials defend the new policies, saying they respond to cancer doctors’ concerns that the agency has been too slow to recognize promising new off-label treatments. Dr. Steve Phurrough, who has overseen coverage for the agency since 2003, noted that a 1993 federal law gave Medicare specific authorization to cover some unapproved uses of cancer drugs.

“Congress wanted a lesser level of evidence,” Dr. Phurrough said. The question of what is adequate evidence is “not a line in the sand,” he said. “It’s a broad stripe in the sand.” The American Society of Clinical Oncology, which represents cancer doctors, has hailed the new rules, saying they will ensure that the appropriate off-label uses are covered.

In 1993, Congress had authorized three reference guides – or compendiums – for Medicare, all published by not-for-profit organizations. The writers and editors of these compendiums, who work completely outside the federal government, scan the medical literature and evaluate the evidence in making their recommendations.

But by 2007 two had stopped publishing, leaving Medicare with a single compendium. The new rules expand the number of compendiums Medicare relies on for determining which off-label uses of cancer drugs to cover. Under the old rules, Medicare representatives were supposed to consult the compendiums but also use their own discretion in interpreting the guides’ recommendations. The new rules essentially delegate the decision to guides Medicare has selected, even when there is little clinical evidence

behind a particular recommendation.

As long as at least one of them recommends a cancer treatment, Medicare is essentially obliged to pay for it – unless one of the other guides specifically advises against it.

And some of these new compendiums have close financial ties to the drug industry, according to the draft of a report Medicare commissioned last year after Congress raised questions about possible conflicts of interest. The draft was completed in October, with a final version to be released soon. The draft criticizes the new rules for essentially taking most decisions about off-label cancer drugs out of Medicare’s hands, even when the agency is aware of potential conflicts. The guide’s recommendation, the report says, “becomes the final word.”

Many oncologists say they needed greater flexibility in using cancer drugs because it can take months or years for a new use to be approved by the FDA. They cite the example of Celgene’s drug thalidomide, now a mainstay treatment for multiple myeloma, which was prescribed only off-label for years before the FDA formally approved it for that use.

And in the case of rare types of cancer, there may be so few potential patients that companies have little financial incentive to undergo the formal FDA process of drug approval. For example, only two drugs are FDA approved for treating brain cancer, and cancer doctors say they need the ability to try other drugs or other combinations of treatments. “To arbitrarily stop after two drugs to me is ludicrous,” especially for younger patients, said Dr. Virginia Stark-Vance, a solo practitioner in Dallas and Fort Worth. She said one of her brain cancer patients had been kept alive for 10 years by off-label use of irinotecan, the ninth drug the patient tried.

Medicare officials acknowledge that some of the potential conflicts need to be addressed. But they say they have confidence in the guides they have chosen. “We had significant conversations with all the companies,” Dr. Phurrough said.

The New York Times, 27 January 2009

ADJUVANT RADIOTHERAPY IMPROVES SURVIVAL AFTER RADICAL PROSTATECTOMY

In a multi-institution study, Ian M. Thompson, MD and colleagues at the University of Texas Health Science Center at San Antonio demonstrated that adjuvant radiotherapy significantly improves survival after radical prostatectomy in patients with advanced prostate cancer. In this study of 425 men with aggressive prostate cancer initiated in 1988, 211 were observed after surgery for signs of recurrence, and 214 received adjuvant radiotherapy shortly after surgery. Unlike most studies which have based results on PSA recurrence, this study’s endpoint was development of metastatic disease.

When data were most recently evaluated in 2008 after an average 12.7 year follow-up, radiation was found to significantly reduce the risk of metastases by 29% and significantly improved survival by 28%. In addition to the most important outcomes of prostate cancer (metastases and survival), the risk of a detectable PSA after surgery (the first evidence of disease recurrence) was reduced by 58% and delayed by more than 7 years. The authors found that all risk groups studied appeared to benefit.

Radiation therapy also significantly reduced the need for hormone therapy after surgery, a treatment which can have profound negative impacts on quality of life. Using measures of quality of life, the study found increases in patients’ urinary and bowel symptoms in the radiotherapy group at six weeks and two years, but these differences subsequently disappeared.

Dr. Thompson commented that “Adjuvant radiotherapy within 18 weeks after radical prostatectomy in a man with pT3N0M0 prostate cancer significantly reduces the risk of PSA recurrence, metastasis and the need for hormonal therapy, and significantly increases survival. All of the approximate 30,000 men each year that face this condition should be informed of the results of this study.”

Journal of Urology, 22 January 2009

PROSTATE CANCER ‘MAN-O-GRAM’ *(Continued from page 1)*

researchers about whether PSA screening actually saves lives, with many arguing that it leads to unnecessary surgical and radiation treatment for minor cancers, causing negative side effects. And because there is no reliable imaging technique to guide the selection of tissue for the biopsies, doctors take random plugs of prostate blindly and may miss tumors.

“Right now what is done essentially is barbaric,” Shtern said in a telephone interview. “We need to be able to find the cancers that are there that are going to be significant – and only target those,” stated Dr. Thomas Wheeler of Baylor College of Medicine in Houston, one of the experts, interviewed.

NEGLECTING ILLNESSES

(Continued from page 1)

with prostate cancer from 1988 through 2002. Overall, 59.1 percent of the entire group had early-stage prostate cancer with low- to moderate-grade tumors.

The mortality in these patients was similar to that of men the same age without prostate cancer. Among the men with early-stage, low- or moderate-grade tumors, mortality from prostate cancer was 2.1 percent versus 6.4 percent from heart disease, and 3.8 percent from other cancers.

The “substantial effect” of other illnesses on survival and the high mortality rate from causes other than prostate cancer may have important implications, Goodwin’s team notes.

Treatment decisions for localized prostate cancer should consider life expectancy based on age and the contribution of other conditions to the patient’s mortality, they note. Also, the decision to use androgen deprivation therapy, which is now commonly used to treat even early-stage prostate cancer, must be made carefully if another significant illness is present. With this approach, androgen, a male sex hormone that can stimulate prostate growth, is blocked.

Overall, they conclude that older men with early-stage prostate cancer “would be well served by an ongoing focus on screening and prevention of cardiovascular disease and other cancers.”

Reuters Health, 27 January 2009

More than two dozen experts from institutions including Johns Hopkins University, Harvard Medical School, the University of Chicago, the University of Miami and Stanford University, joined the effort. They signed letters to Congress and the US National Institutes of Health saying more accurate imaging technology would lead to better guidance for diagnosis, biopsy and minimally invasive treatment.

Shtern said there needs to be a better initial screening test than the PSA test, perhaps a new blood or urine test focused on another biological indicator of prostate cancer.

Reuters, 14 January 2009

FAMILY HISTORY OF PROSTATE CANCER DOES NOT AFFECT TREATMENT OUTCOMES

In a first of its kind study, a first-degree family history of prostate cancer has no impact on the treatment outcomes of prostate cancer patients treated with brachytherapy (also called seed implants), and patients with this type of family history have clinical and pathologic characteristics similar to men with no family history at all, according to a January 1st study in the *International Journal of Radiation Oncology*.

According to the American Cancer Society, many patients diagnosed with prostate cancer have some type of family history of the disease. Men with a family history do have an increased risk of developing the disease, but there is conflicting data on how family history impacts treatment outcomes.

In the study, researchers at Mount Sinai School of Medicine in New York sought to determine if having a familial history of prostate cancer, which is defined as a clustering of prostate cancer cases within a family, had an impact on the prognosis of men treated with brachytherapy for clinically localized prostate cancer.

Researchers followed 1,738 prostate cancer patients, of which 187 had a family history of prostate cancer in a first-degree relative, for a median of 60 months. They found that in low-, intermediate- and high-risk groups, family history had little to no prognostic significance in men treated with brachytherapy. Previous studies done using external beam radiation therapy or radical prostatectomy had similar findings.

“This information is relevant for both physicians and patients with new diagnoses as they embark on complex treatment decisions,” said Christopher A. Peters, MD, lead author and a radiation oncologist at Northeast Radiation Oncology Center in Dunmore, PA (chief resident at Mount Sinai at the time of the study).

“Now patients with a family history of prostate cancer can be confident that they have the same outcomes as patients with sporadic disease, regardless of the treatment modality they chose.”

Science Daily, 2 January 2009

DONATED ITEMS SOUGHT FOR JUNE 2009 US TOO ONLINE AUCTION

Us TOO International will host our fourth annual online auction, June 8-23, ending the Tuesday after Father’s Day weekend, to honor fathers who either have had prostate cancer or who are trying to stay prostate-healthy.

In advance of the auction, Us TOO is seeking donated items from individuals, companies and chapters for bid. Ideas for items can range anywhere from tickets to a professional sports event or show, a flat screen TV, an iPod, a unique or limited edition item, collectibles, gift baskets, etc. Think what appeals to consumers. Think what appeals to you! A range of price points are needed. Items could appeal to men, women, young adults or children.

For each item donated, the following information is needed: a photo, short description, regular price or value, and name of the item donor if he/she wants to be recognized.

To donate an item, please contact Ryan Maguire at ryan@ustoo.org or by phone at 630-795-1002.



**DOC MOYAD'S WHAT WORKS & WHAT IS WORTHLESS
COLUMN ALSO KNOWN AS "NO BOGUS SCIENCE" COLUMN**

**"Androgen deprivation therapy causes cardiovascular disease?
Maybe not!"**

Mark A. Moyad, MD, MPH
University of Michigan Medical Center, Department of Urology

Bottom Line:

Androgen Deprivation Therapy (ADT) does not appear to increase the risk of cardiovascular death in men with locally advanced prostate cancer. The adverse effects of ADT require close monitoring, but the apparent risk of cardiovascular death may have been overestimated.

ADT, especially LHRH agonists have been around for over 20 years, and the issue is no longer whether or not they reduce the risk of death from prostate cancer (we know they do). The current issue is the potential side effects, some minor, and some major that may occur with long-term use of these products.

The largest concern has to be whether or not ADT increases cardiovascular mortality. This issue goes round and round and is debated, but where is the real evidence ladies and germs? (That is a tribute to my 12-grade biology teacher that use to always say that!)

Researchers analyzed retrospectively the risk of death from cardiovascular causes from the famous randomized trial RTOG 92-02. This trial primarily compared the impact of short (4 months) versus long-term (28 months) ADT in men with locally advanced prostate cancer receiving radiation treatment. The average age of the men was 70 years and follow-up was approximately 8.1 years and 185 cardiovascular deaths occurred during the trial, and 765 total deaths (24%) occurred out of a total of 1554 men that began the trial.¹

At 5 years, there was no significant difference in cardiovascular deaths between the long (5.9%) and short-term (4.8%) ADT arms. Age, diabetes or previous cardiovascular disease were more important predictors of cardiovascular mortality, but ADT duration was not associated with cardiovascular mortality regardless of how the definition of heart disease was

perceived.

In fact, significantly more patients in the long-term ADT arm (30%) began the trial with a history of cardiovascular disease compared to the short-term arm (25%, p=0.03), but there was still no difference in cardiac deaths with ADT. In addition, all randomized trials or prospective studies completed thus far have currently been unable to find a significant or consistent increase risk of cardiovascular mortality with ADT.

However, it is true that ADT may cause weight gain, glucose changes and possibly triglyceride increases, so this may increase the risk of what is known as "metabolic syndrome" and heart disease, especially in a high-risk cardiac patient.

Regardless, as long as cardiovascular disease is the number 1 cause of death in men with and without prostate cancer, I have always believed that men treated for localized or locally advanced prostate cancer need to do whatever is needed to reduce their risk of cardiovascular disease and death to as close to zero as possible. This means low cholesterol and blood pressure, regular aerobic exercise, weight lifting, good diet, good beer blah, blah, blah – you've already heard it from me enough times so I will end here!

Reference:

1. Efstathiou JA, Bae K, Shipley WU, Hanks GE, Pilepich MV, Sandler HM, Smith MR. Cardiovascular mortality and duration of androgen deprivation for locally advanced prostate cancer: analysis of RTOG 92-02. *Eur Urol* **54**:816-24, 2008.

PS If the Michigan basketball team gets a bid to the NCAA basketball tournament, I will buy everyone at the Us TOO home office a beer.

**NOVEL ANDROGEN
RECEPTOR VARIANTS TIED
TO HORMONE-REFRACTORY
PROSTATE CANCER**

In a report in the January 1st issue of *Cancer Research* (Vol. 69, pp. 1-7, 2009), the researchers describe the discovery of seven novel androgen receptor (AR) variants that are prevalent in hormone-refractory prostate cancer. They focused their attention on the two most abundantly expressed variants, AR-V1 and AR-V7. AR-V1 and AR-V7 mRNA "showed an average 20-fold higher expression" in 25 hormone-refractory prostate cancer tissue specimens when compared with 82 hormone-naive prostate cancer specimens (p < 0.0001), Dr. Jun Luo and colleagues report from The Johns Hopkins University School of Medicine, Baltimore, MD.

A subset of hormone-naive prostate cancer specimens expressed AR variants at levels comparable with those in hormone-refractory prostate cancer specimens, and elevated AR-V7 expression predicted biochemical recurrence (indicated by PSA levels) after surgery, they also report.

The team generated polyclonal antibodies against AR-V7 and found that these antibodies detected the AR-V7 protein "frequently" in hormone-refractory prostate cancer specimens but rarely in hormone-naive prostate cancer specimens. In lab-grown androgen-depleted prostate cancer cells made to produce only the AR-V7 variant, AR-V7 was constitutively active in driving the expression of at least 20 androgen-responsive genes.

"This study uncovered the genetic codes of multiple new androgen receptors that somehow manage to keep the androgenic signaling pathway going without being tagged by androgens Dr. Luo noted." This discovery may help us better understand why prostate cancer cells escape hormone treatment, designed to interrupt the androgenic signaling pathway, and eventually become refractory to therapies," he added.

"These new receptors may be targeted for developing assays to predict and track the effectiveness of hormone therapy or used to develop new drugs."

Reuters Health, 7 January 2009

THE DOCTORS NOTE

Dr. Gerald Chodak

This month's *HotSheet* shows us that politics also extends into the medical arena. An issue likely to affect men with prostate cancer is the decision by Medicare to cover off label use of drugs used to treat cancer. For patients no longer responding to approved medications, this offers the opportunity to receive medications that have not gone through proper scientific studies yet may still be helpful in some cases. However, aside from the large federal expense that may result, the real downside to this policy is that it will discourage patients from participating and doctors from performing proper clinical studies aimed at determining if the drugs really are effective work for the off-label disease. In the end, some patients may benefit but many more will be worse off by receiving medications that do not significantly improve survival.

One example is the use of Thalidomide which has some new data from a randomized study (p2) showing it increases PSA progression free survival in men with PSA recurrent disease. Some would argue that this evidence is enough to justify its being used routinely in this disease. And yet, many of the men enrolled in this study were unlikely to ever need treatment and PSA recurrence is still not correlated with an improvement in survival. With the new Medicare funding rule, doctors are likely to increasingly use Thalidomide and avoid having patients enroll in studies aimed at determining if it improves survival or delays metastases.

A second issue is the appeal for funding a search for a 'man-o-gram' to determine if expensive ultrasound or MRI imaging will do for men what the mammogram does for women, namely screen for prostate cancer. This is certainly to be controversial given the unresolved controversy over screening for prostate cancer using the PSA which has been under investigation for nearly 13 years and has not yet proven that it saves lives. Given the HUGE budget deficits we are facing, will this added expense be a worthwhile use of taxpayer dollars over other health efforts, especially for men over 50 who have prostate cancer yet never know the even have the disease?

Another controversy brought out this month is the question whether immediate ADT improves survival in men found to have lymph node metastases following radical prostatectomy. A retrospective, uncontrolled study was recently published that showed it did not improve survival. To date, only one prospective randomized study has been published and it did show a significant improvement. Although that study was criticized for not enrolling its intended number of patients, it still is the best information available and the design of this new report is so full of potential biases it does not serve as a valid refutation of the previous report. Until a new proper randomized study is performed (which is certainly warranted), patients should still be told that immediate hormone therapy is the best way to prolong their survival if they are found to have lymph node metastases.

A very important finding is the latest update on a prospective study aimed at determining if men with tumor outside the capsule at surgery (pT3 disease) benefit from post-operative radiation. Until now, this study did not show an improvement in survival, but with further follow-up of more than 12 years survival was indeed increased. This finding means that men with pT3 disease can now be counseled that radiation is truly worthwhile in this setting. Yet again, this study is evidence of the need to study these questions using a proper study design.

Lastly, interesting data about the breast cancer genes BRCA1 and BRCA2 may stimulate further research into determining which men screened for prostate cancer are good or bad candidates for expectant/delayed therapy. These genes are helpful for identifying which women have aggressive breast cancer. The new finding suggests that if these genes are present in men with prostate cancer, the disease is more aggressive, meaning that they would not be good candidates for conservative therapy. This finding needs to be studied in those men around the country who have not received definitive therapy to see if the finding has real merit. If so, it could be a major step forward in selecting the right men for aggressive treatment.

ADJUVANT ANDROGEN DEPRIVATION NOT CLEARLY BENEFICIAL IN NODE-POSITIVE PROSTATE CANCER

In men with node-positive prostate cancer, beginning or deferring adjuvant androgen deprivation therapy (ADT) after surgery does not appear to significantly impact survival, according to a report in the January issue of the *Journal of Clinical Oncology* (Vol. 27, pp. 100-5, 2009).

Dr. Yu-Ning Wong at the Fox Chase Cancer Center in Philadelphia and colleagues came to this conclusion after analyzing Surveillance, Epidemiology and End Results (SEER) and Medicare data on 731 men who underwent radical prostatectomy between 1991 and 1999 and had positive regional lymph nodes.

There was no statistically significant difference in overall survival between the 209 men who received ADT within 120 days after surgery and the 522 men who did not. There was also no statistically significant survival differences with 90, 150, 180, and 365 days as the adjuvant therapy definition, according to the researchers.

"Our study highlights the significant uncertainty that surrounds the role of adjuvant therapy for men with high-risk, localized prostate cancer," the authors write.

They point out that while ADT has not been effective when performed prior to prostatectomy, it "has a well-defined role" in patients with locally advanced prostate cancer who are receiving definitive radiation therapy. "This apparent dichotomy may support an interaction between radiation therapy and ADT," they speculate. "This may also explain the lack of benefit of adjuvant ADT seen in this study."

Dr. Wong and colleagues acknowledge that the findings of this observational study should be validated in a prospective study. Nevertheless, they add, "We believe that these results add to the currently available data and should help treatment decisions, especially in patients who are concerned about ADT-associated toxicity."

Reuters, 31 December 2008

ADVOCACY ALERT

Thomas N. Kirk, President & CEO, Us TOO International

As you know, Us TOO's mission and priorities are summarized in our SEA Blue campaign to Support, Educate and Advocate. I am sure you have noted change is in the air in Washington, DC now that President Obama has been sworn in and the 111th Congress is in session. How do we plan to have impact for Prostate cancer in this new environment?

One way is that the Prostate groups are working more closely together than ever before, and we are asking all of us to get more involved during 2009. Look for more advocacy information and resources from emails, websites and in newsletters like the *HotSheet*. And take action where you feel comfortable to make your voice heard, voices need to be heard to impact funding levels.

You will be receiving information on priority areas of focus such as the DOD Congressionally Directed Medical Research Programs (CDMRP). Started in 1992, the CDMRP now administers programs funding breast cancer, prostate cancer, ovarian cancer, chronic myelogenous leukemia, neurofibromatosis, and tuberous sclerosis research. The Prostate Cancer Research Program at DOD is the only federal program that is 100% dedicated to prostate cancer research.

The prostate cancer community has struggled to conduct human clinical trials and level funding for the past 8 years (\$85 million from FY2002-FY2005 and \$80 million from FY2006-FY2009) combined with increases in indirect costs and other inflation-related issues have resulted in a net decrease in direct funding for prostate cancer research, and the program cannot directly fund clinical trials in fiscal year 2009.

As a sign of growing consensus, the Prostate cancer groups all agree to request that \$125 million be allocated to the Prostate Cancer Research Program at the Department of Defense in the months ahead when budget decisions are made.

Look for the information that is available on this priority advocacy issue, get informed and empowered so we can push for more research to find the solutions and answers we need.

EXPERT: CONGRESS COULD CONTROL RAPIDLY RISING CANCER DRUG COSTS

The government today can do little to stop the rapid and dramatic rise in the cost of cancer drugs, which is forcing many patients to pay thousands of dollars out-of-pocket for treatment, according to an analysis published online on 27 January 2009 in *The New England Journal of Medicine*.

But Congress could change that, says author Dr. Peter Bach, a former senior policy adviser to the Centers for Medicare and Medicaid Services. The government pays for the bulk of cancer care, through programs such as Medicare, Medicaid and the Department of Veterans Affairs.

One way to control rising drug prices is to create a "comparative effectiveness center." Doctors at that center could determine which cancer drugs work best for particular patients – and which are a waste of money. Congress should allow the Medicare program to use this information when deciding which drugs to pay for, says Bach, an epidemiologist, pulmonary and critical care physician at Memorial Sloan-Kettering Cancer Center. If scientists find that several drugs work equally well, Medicare could negotiate with manufacturers to try to find the best price.

The Medicare program already makes these kinds of decisions for other conditions and drugs, such as treatments for emphysema, Bach says. The stimulus package being debated in the House of Representatives includes this kind of drug research center.

Download the full report at no cost at <<http://content.nejm.org/cgi/content/full/NEJMp0807774?query=TOC>>.

USA Today, 27 January 2009

THALIDOMIDE

(Continued from page 2)

treated men. Fatigue was also common, occurring in 19% of thalidomide-treated men and in 11% of placebo-treated men. Larger studies with longer follow-ups are needed to determine the usefulness of thalidomide in this setting, note the study authors.

Despite his criticisms, Dr. Beer praised the researchers for the novel approach to treatment in the study and endorsed the idea of attempting to improve ADT. "Enhancement of hormonal therapy has great potential to improve outcomes in early- and late-stage prostate cancer," he writes. The potential is greater than that of chemotherapy, he notes, which has a much lower median time to progression (about 6 months) than hormonal therapy, with its median time to progression ranging from 16 to 48 months.

Study coauthor Philip M. Arlen, MD, from the Laboratory of Tumor Immunology and Biology, NCI, NIH, in Bethesda, MD, has a financial interest or relationship with Neogenix Oncology.

Medscape, 28 January 2009

BREAST CANCER MUTATION RAISES PROSTATE RISKS IN MEN

The so-called breast cancer genes BRCA1 and BRCA2 can raise the risk that a man who develops prostate cancer will get an aggressive form of the disease, US researchers recently reported. Certain mutations in the genes indicated a man was at risk of more aggressive cancer and should be treated right away, the team at the Albert Einstein College of Medicine of Yeshiva University said. Their study of 2,000 Jewish men shows the gene mutation, more common among Jews of European descent, might help show which men have a slow-growing tumor that may not need immediate treatment.

For their study, Burk and colleagues tested 979 men with prostate cancer and 1,251 men without it for BRCA1 and BRCA2, both rare genetic mutations known in women to raise the risk of breast and ovarian cancers consid-

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**PROSTATE CANCER AGGRESSIVENESS
LINKED TO GLAND SIZE**

Two new studies provide further evidence that prostate cancer patients having small prostates are more likely to have positive surgical margins and other evidence of higher-risk tumors.

Researchers reviewed the records of 1,296 patients who underwent robotic-assisted laparoscopic prostatectomy at New York Presbyterian Hospital. Smaller prostates were significantly associated with a higher risk of positive surgical margins. The positive surgical margin rate was 10.9% for men with prostates weighing ≤ 50 gm versus 7.2% for prostates > 50 gm, a significant difference between groups. Positive margins also were significantly associated with higher pre-op PSA levels and Gleason sum on final histology.

Gerald Y. Tan, MD, of the Weill Medical College of Cornell University in New York and colleagues noted that their findings mirror those of a study led by Stephen J. Freedland, MD, then of Johns Hopkins School of Medicine in Baltimore (*J Clin Oncol*; 23:7546-54, 2005). The study showed that men with smaller prostates had more high-grade cancers and more advanced disease and were at greater risk of pro-

gression after radical prostatectomy. Like Dr. Freedland, Dr. Tan agrees with the hypothesis that for a given age, a small prostate with the same PSA as a larger gland is likely associated with aggressive cancers.

“Accurate preoperative assessment of prostate weight may help surgeons better predict who is likely to have more aggressive disease on final pathology and help them adjust their operative strategies for cancer clearance accordingly,” said Dr. Tan.

In another report, German and Turkish researchers analyzed records of 71 men with small prostates (≤ 25 cm³) and 76 men with large prostates (≥ 75 cm³) who underwent laparoscopic radical prostatectomy. The rate of positive surgical margins was 21% in the ≤ 25 cm³ group compared with 8% in the ≥ 75 cm³ group. Moreover, a higher proportion of men with small prostates presented with non-organ-confined tumors (47% vs. 29%), a Gleason score ≥ 7 (59% vs. 33%), and biochemical recurrence (24% vs. 5%). All between-groups differences were significant.

Renal & Urology News, 21 January 2009

BRCA-1 AND BRCA-2

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erably. Men with any one of three mutations in the two genes were not any more likely to be in the prostate cancer group. But, if they did have one, their cancer was much more likely to be of an aggressive type, Burk’s team reported in the journal *Clinical Cancer Research*.

“One of the biggest problems with early-stage prostate cancer is being able to distinguish between tumors with the potential to become aggressive and those that may persist for many years without enlarging or spreading,” said Dr. Robert Burk, who led the study. “Our large study shows conclusively that prostate cancer patients with either the BRCA2 gene mutation or the BRCA1-185delAG mutation are more susceptible to aggressive cancers than people without that mutation,” Burk added.

He stated that Ashkenazi Jewish men diagnosed with early-stage prostate cancer might want to consider getting tested for the mutations in BRCA2 and BRCA1 genes.

Reuters, 29 January 2009

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