Newsletter

Prostate Cancer 101, Inc.

http://prostatecancer101.org

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The Prostate Cancer Information and Support Group of the Mid-Hudson

Nanoparticle PSA Test Predicts If Prostate Cancer Will Return; Ultrasensitive Test Gives First Accurate Answer After Surgery

by Alton Parrish | BeforeItsNews.com | 06.02.2010

Men who have just had their cancerous prostate gland removed have one pressing question for their doctors: Am I cured? But conventional tests haven't been sensitive enough to provide a concrete answer.

Current tests that measure the level of protein called PSA (prostate-specific antigen), which signals the presence of cancer, often detect no PSA, only to have cancer return in up to 40 percent of the cases.

New research from Northwestern University Feinberg School of Medicine and the University International Institute for Nanotechnology shows that an ultrasensitive PSA test using nanoparticle-based technology (VeriSens™ PSA, Nanosphere, Inc., research-use-only) may be able to definitively predict after surgery if the cancer is cured long-term or if it will recur.

The new test, which is based upon assays invented at Northwestern in the laboratories of co-principal investigator Chad A. Mirkin, is 300 times more sensitive than currently available commercial tests and can detect a very low level of PSA that indicates the cancer has spread beyond the prostate. The test also may pick up cancer recurrence at a much earlier stage, when secondary treatment is most effective for a patient's survival.

"This test may provide early and more accurate answers," said co-principal investigator C. Shad Thaxton, M.D., an assistant professor of urology at Feinberg and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

"It detects PSA at levels in the blood that cannot be detected by conventional tests. It may allow physicians to act at the earliest and most sensitive time, which we know will provide the patient with the best chance of long-term survival."

This ability to quickly detect very low levels of PSA may enable doctors to diagnose men with prostate cancer recurrence years earlier than is currently possible. Prostate cancer is the second leading cause of cancer death for men in the United States.

Not only may the new test more accurately predict the course of the disease; it also gives an early indication of whether secondary treatments, such as radiation and hormone therapy, are working. If not, then doctors can quickly begin alternative treatment and refer patients to clinical trials.

The study results will be presented at the American Urologi-

cal Association 2010 Annual Meeting. These and the results of other Northwestern PSA studies will be presented at the meeting by Lee Zhao, Dae Kim and Hannah Alphs, urology residents at Feinberg.

"These studies suggest that the nanotechnology PSA test might become the preferred postoperative PSA test for men who have been treated with radical prostatectomy," said William Catalona, M.D., professor of urology at Feinberg, a physician at Northwestern Memorial Hospital and director of the clinical prostate cancer program at the Lurie Cancer Center.

"It should be especially useful in the early identification of men who would benefit from adjuvant postoperative radiation therapy and those who need postoperative salvage radiation therapy for recurrence."

Catalona, a senior investigator on the study, was the first to demonstrate that the PSA test could be used as a screening test for prostate cancer.

The study confirms and builds on the previous findings of a 2009 pilot study Thaxton conducted with Mirkin, the George B. Rathmann Professor of Chemistry in the Weinberg College of Arts and Sciences, and other colleagues.

PSA is a protein normally secreted out of the prostate cells into the semen in high concentrations. Usually, very little diffuses into the blood stream, and the normal PSA value for men without prostate disease is less than 2 nanograms per milliliter.

When the prostate gland has a disease process, such as inflammation, benign enlargement or cancer, the barriers to PSA diffusion into the blood stream are breached, and PSA levels rise.

In a man who has his cancerous prostate removed, there should be no PSA in the blood except for a minute amount produced by the periurethral glands. However, any PSA produced by cancer recurrence ends up in the blood stream and can be detected earlier with the more sensitive nanotechnology PSA assay.

For the new study, researchers obtained blood serum retrospectively from men whose PSA serum samples had been frozen after surgery and whose assays (blood analysis) showed an undetectable PSA level based on the conventional test.

Northwestern researchers then tested those serum samples using the more sensitive nanotechnology-based test. They wanted to see if they could detect PSA at levels below the limit of the conventional test, and if those results could predict the cancer outcome for those patients, who were followed for up to 10 years.

Using the new test, Thaxton and colleagues found that the low and non-rising PSA levels (presumably produced by the normal periurethral glands) of patients meant that the prostate cancer was effectively cured and did not return over a period of at least 10 years. Scientists also found a PSA level higher than that expected from the periurethral glands based on the new test meant the patients would have their disease recur.

As result of the study, researchers were able to assign a PSA level number to a cure for the first time as well as a number that indicated the disease would recur and if it would recur aggressively.

These newly identified levels were below what could have been detected with the conventional PSA test. The researchers were able to quantify PSA values at less than 0.1 nanograms per milliliter, the clinical limit of detection for commercial assays.

Thaxton said the next step for scientists is a prospective clinical trial to compare the nanoparticle-enhanced PSA assay to traditional PSA assays and determine if earlier detection and treatment can save lives.

Source: ZERO – The Project to End Prostate Cancer

Protect Your Erection: 11 Tips
How to avoid erectile dysfunction and protect your potency.

By David Freeman

WebMD Feature Reviewed by Laura J. Martin, MD

Erectile dysfunction (ED) is common in older men. But it's not a normal part of aging. How can you avoid ED? Here's what experts told WebMD.

1. Watch what you eat.

A diet that's bad for a man's heart is also bad for his ability to have erections.

Research has shown that the same eating pattern that can cause heart attacks by impeding blood flow in the coronary arteries -- few fruits and vegetables and lots of fatty, fried, and processed foods -- can impede blood flow to and within the penis. That blood flow is needed for the penis to become erect.

Anything that is bad for a man's heart is also bad for his penis, says Andrew McCullough, MD, associate professor of clinical urology and director of the male sexual health program at New York University Langone Medical Center.

Recent studies show that ED is relatively uncommon among men who eat a traditional Mediterranean diet, which includes fruits, vegetables, whole grains, heart-healthy fats including nuts and olive oil, fish, and wine.

"The link between the Mediterranean diet and improved sexual function has been scientifically established," says Irwin Goldstein, MD, director of sexual medicine at Alvarado Hospital in San Diego.

2. Maintain a healthy weight.

Being overweight can bring many health problems, including type 2 diabetes, which can cause nerve damage throughout the body. If that affects the nerves affecting the penis, ED can result.

3. Avoid high blood pressure and high cholesterol.

High cholesterol or high blood pressure can damage blood vessels, including those that bring blood to the penis. Eventually, this can lead to ED.

Make sure your doctor checks your cholesterol levels and blood pressure. You might also want to check your blood pressure between doctor visits. Some stores and fire stations offer free screening; blood pressure monitors are also sold for home use.

If your cholesterol or blood pressure is out of whack, get it treated.

Blood pressure drugs can make it hard to get an erection. But doctors say many cases of ED that get blamed on these drugs are actually caused by arterial damage resulting from high blood pressure (also called hypertension).

4. Drink alcohol in moderation or not at all.

There is no evidence that mild or even moderate alcohol consumption is bad for erectile function," Sharlip says. But chronic heavy drinking can cause liver damage, nerve damage, and other conditions that can lead to ED.

5. Exercise regularly.

Strong evidence links a sedentary lifestyle to erectile dysfunction. Running, swimming, and other forms of aerobic exercise have been shown to help prevent ED.

Watch out for any form of exercise that puts excessive pressure on the perineum, which is the area between the scrotum and anus. Goldstein says bicycle riding, in particular, can cause ED.

An occasional short ride is unlikely to cause trouble. But men who spend a lot of time biking should make sure their bike fits them properly, wear padded cycling pants, and stand up frequently while pedaling.

"No-nose" bike seats protect against genital numbness and sexual dysfunction, according to the National Institute for Occupational Safety and Health.

6. Don't rely on Kegels.
One form of exercise that doesn't seem helpful is Kegel exercises, which involve repeatedly contracting and relaxing the muscles in the pelvis. Kegels can be helpful for men and women suffering from incontinence. But there's no evidence that they prevent erectile dysfunction.

7. Keep tabs on testosterone.
Even in healthy men, testosterone levels often begin falling sharply around age 50. Every year after age 40, a man's testosterone level typically falls about 1.3%.

Symptoms like a low sex drive, moodiness, lack of stamina, or trouble making decisions suggest a testosterone deficiency, as do spongy erections. Your doctor can check on that.

8. Avoid anabolic steroids.
These drugs, which are often abused by athletes and bodybuilders, can shrink the testicles and sap their ability to make testosterone.

9. If you smoke, stop.
Smoking cigarettes can harm blood vessels and curb blood flow to the penis. And nicotine makes blood vessels contract, which can hamper blood flow to the penis.

10. Steer clear of risky sex.
Some cases of erectile dysfunction stem from penile injuries that occur during sex. To keep your penis from bending painfully, start thrusting only after making sure her vagina is well lubricated. And make sure your penis doesn't slip out of the vagina while thrusting (so you won't accidentally jam your penis against a hard part of her body). If she moves in such a way that hurts your penis -- for instance, by bending it the wrong way -- have her stop at once.

"If the woman is on top and comes down hard, and the penis does not enter the vagina, that is the equivalent of a big weight crashing down on the penis," Goldstein says. "No penis on earth can withstand that."

11. Curb stress.
Psychological stress boosts levels of the hormone adrenaline, which makes blood vessels contract. That can be bad news for an erection. Anything a man can do to ease tension and feel better emotionally is likely to give his sex life a big boost.

Source: www.webmd.com

Thank you all for your Contributions

Douglas & Nancy McBride
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Joseph & Helen Sullivan
Leroy & Janie Wilcox

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"You don't lead by hitting people over the head-that's assault, not leadership"

Dwight Eisenhower

"Courage is being scared to death—but saddling up anyway"

John Wayne

"The secret of success is honesty and fair dealing. If you can fake those, you've got it made"

Groucho Marx

Experts Discuss the Current State of Cancer Clinical Trials
Physician and patient participation is a major issue, but there are other areas of concern as well.

by Leah Lawrence | HemOnc Today | 05.25.2010

In 2009, about 1.5 million people were diagnosed with cancer, according to the American Cancer Society's Cancer Facts & Figures 2009. However, research continues to show that fewer than 10% of adults diagnosed with cancer participate in clinical trials.

Barriers to clinical trial participation — by patients and physicians — have been identified as a major issue, but other problems may exist within the framework of the clinical trials process in the United States, according to the experts interviewed by HemOnc Today.

"The clinical trial process is the best mechanism to provide legitimate evidence that medical progress has been made," said Laurence H. Baker, DO, professor of medicine at the University of Michigan and chair of the Southwest Oncology Group.

However, Baker also said asking whether or not the clinical trials process is working is an extraordinarily complicated question, and "there are many problems with clinical trials in this country as they relate to cancer."

"I believe that the American public is terribly frustrated with our lack of progress," he told HemOnc Today.

Organizations such as the National Cancer Institute and American Society of Clinical Oncology continue to advocate and develop new programs and partnerships to try to increase enrollment in clinical trials, particularly by underrepresented populations. These organizations said if adult enrollment in clinical trials was higher, greater knowledge about possible beneficial treatments could be discovered at an increasingly rapid pace.

In fact, the Institute of Medicine (IOM) published a report in April calling for a "reinvigoration" of the NCI Cooperative Group Program. In the report, the IOM supported the NCI Clinical Trials Cooperative Group Program for its key role in developing new cancer therapies but said in recent years, "many stakeholders — including clinical investigators, patient advocates, Cooperative Group leadership, industry participants as well as the NCI — have expressed concerns that the program is falling short of its potential to conduct the timely, large-scale, innovative trials needed to improve patient care."

Among the IOM's goals for reinvigoration were an improvement in the participation of patients and physicians and an increase in the support of clinical trials.

Increasing enrollment

The bar for a successful clinical trials process has been set in the childhood cancer arena, in which the process is decidedly different and historically more successful. According to the ACS, each year about 10,000 children are diagnosed with cancer and about 4,000 enroll in a clinical trial. Cure rates for childhood cancers are about 80%.

"In pediatrics, we have a longstanding history of being able to recruit children to clinical trials," said Gregory H. Reaman, MD, of Children's National Medical Center, Washington, D.C., and chair of the Children's Oncology Group. "It has enabled us to build sequentially, from one trial to another, and improve outcomes for many childhood cancers, most notably acute lymphoblastic leukemia, Wilms' tumor, acute myeloid leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma and neuroblastoma."

Reaman said getting patients to participate in clinical trials is part of the culture of pediatric oncol-

ogy. “It is how we do what we do. As a group, we have understood the importance of collaboration and cooperation,” he said.

In the adult arena, research has shown that a key to enrolling patients into clinical trials is physician participation.

“The physician plays the most important role of anybody,” said Robert L. Comis, MD, president and chairman of the Coalition of Cancer Cooperative Groups and group chair of the ECOG. “The physician is also a patient’s most trusted source of information.”

Comis and colleagues at the Coalition of Cancer Cooperative Groups, a non-profit service organization working to improve physician and patient access to cancer clinical trials, published the results of a study examining the physician’s role in patient enrollment in the Journal of Oncology Practice in 2009. In it, an Internet-based survey was performed to assess public and cancer survivor attitudes toward cancer clinical trials; specifically, the survey examined the role of the physician.

“We asked cancer survivors, and roughly 10% to 15% of them said that they were aware that clinical trials might be an option for them at the time of their diagnosis,” Comis told HemOnc Today. “If you asked them who they learned about clinical trials from, 75% said their physician. The other 25% learned from all different sources — from advocacy groups to nurses — but no group was more than 10%."

“If you asked people who actually participated in a trial, the doctors informing them about the studies, educating them about studies and helping them find studies were all directly correlated with whether or not they participated,” Comis said.

Another Internet-based survey, conducted by Maurie Markman, MD, of The University of Texas M.D. Anderson Cancer Center, and Meredith Grimm, RN, of Medscape CME, found that more than 75% of health care providers said they thought that patients derived benefit from trials, but only 20% to 40% had an awareness of educational resources, physician responsibilities or insurance coverage benefits for patients.

The results of the survey, published on Medscape’s website in October, identified several physician barriers to enrollment, including loss of patients through referral to outside clinics, lack of resources and the increased time commitment by the physician.

“There are many barriers to physician participation that need to be addressed,” Baker said. “One of the principal barriers may be financial. It takes a lot more time for physicians to explain and enroll patients into clinical trials, and there is a lot of pressure on physicians to generate income, whether they are in a solo or group practice, or they work for a university or cancer center.”

Baker said institutions frequently have to supplement the cost of enrolling patients in clinical trials, particularly in cooperative-group trials, because the amount of reimbursement per patient is insufficient.

At The Society for Gynecologic Oncologists’ 2010 Annual Meeting on Women’s Cancer, an abstract was presented that detailed the current costs of conducting a phase-3 Gynecologic Oncology Group (GOG) study compared with the amount of reimbursement provided by the GOG. They found that participants are only reimbursed about 30% of their actual costs.

The researchers established a budget for GOG-218, a randomized trial evaluating carboplatin/paclitaxel with or without bevacizumab (Avastin, Genentech) for the treatment of ovarian cancer.

The cost per patient during the treatment phase of the trial was $5,140. The maintenance phase cost was an extra $3,855 per patient, for a total average cost per patient of $8,995. For the per capita points system, the GOG reimbursed only $2,870

per patient, a significant financial loss.

"The clinical trial process has been suffering for a long time because of insufficient funding," Reaman said. "I think things are only getting worse because of the economic stressors that institutions and physicians are now facing."

In fact, a survey conducted by ASCO and published in the Journal of Oncology Practice found that one-third of NCI Cooperative Group Sites plan to limit participation in federally funded clinical trials. Of the sites planning to limit participation, 75% said it was because of inadequate per-case reimbursement.

Besides financial stressors, physicians also face increased work time, increased paperwork and increased scrutiny, and have to be willing to have records directly audited, Comis said.

"If you go to a physician and say, 'I want you to do this clinical trial, and you are going to make less money to do this trial than if you didn't do it, and you are going to have to work harder and spend more time with patients than if you didn't do this trial …' a lot of physicians, who are already overwhelmed and busy, are going to say sarcastically, 'Where do I sign up?'" said Charles H. Weaver, MD, executive editor of CancerConnect.com, a developer of oncology websites, and Women & Cancer magazine. "People don't like to talk about this situation, but this is the harsh reality."

Patient barriers

"There are many physicians in this country who fervently want to provide new information and new knowledge that will lead to change for the better in prevention and treatment of cancer, and they often use the clinical trial process as a method of achieving those goals," Baker said.

Getting physicians to participate is only the first step, patient barriers to participation also exist. According to the results of another online survey study, published in Community Oncology in May 2009, among patients' most commonly self-reported barriers to clinical trial participation were a lack of awareness of appropriate trials, belief that the current treatment is more effective, a fear of possible adverse effects and a fear of getting placebo.

"Patient barriers start at diagnosis. Their physician may not communicate to them that a clinical trial may be appropriate," Weaver said. "Even if a patient is already aware of clinical trials, their physician may not offer a trial that is relevant to that patient, and patients may not consider that more appropriate treatment may be available somewhere else."

"Even patients who are aware of trials don't always participate," Comis said. "One of the major concerns patients have is that the new treatments on trials may not be as effective as the standard treatments."

Trials have to have value to a patient, besides the "perceived notion of helping their fellow man," Weaver said.

"Patients are interested in getting better care for themselves. If a trial doesn't offer the prospect, convincingly, that participation will give them better care than they can get outside of a trial, it is hard to explain to a patient why else they may want to participate," he said.

However, some trials offer experimental treatments that may be better than the standard of care. "That is an intrinsic part of the trials process," Comis said. Patients may participate in trials to get treatment opportunities that are not available any other way.

Regardless, explaining the issues related to the treatment and toxicity related to any given clinical trial comes down to patient education, according to Comis. "The physician needs to make sure the patient is fully informed," he said.

Placebo-controlled trials

One of the most difficult elements of educating patients is explaining trials involving the use of placebos.

According to Baker, there is still a great mistrust of the trials process among the American public due, in large part, to the fear of placebos.

"I agree with the public and understand that fear," Baker said in an interview. "The way to fix that fear is to do away with placebo studies in which a placebo is the only treatment for cancer. I do not think that it would be ethical to argue that a clinical trial that includes a placebo as the sole treatment of cancer would be in keeping with my understanding of my obligation to a patient."

Eliminating placebo-controlled trials may be easier in theory than practice. Currently, the gold standard trial design for FDA regulatory approval is a phase-3, randomized, placebo-controlled study.

"You have a national cancer infrastructure that is vested in pursuing this strategy of drug development," Weaver said. "The experimental arm of the phase-3 trial has to be significantly more appealing or provide access to a drug that a patient could not otherwise access in order to have a patient want to go through with the trial."

"If I tell you that the standard of care is 'X' and the experimental arm is 'X' plus 'Y,' and all of the phase-2 data says there might be a modest benefit at best, or the treatments might be equivalent, a patient would likely ask, 'Why would I want to participate in this trial if it is not going to benefit me?" he said.

Larger, sequential, appropriately conducted phase-2 studies, which do not involve placebo arms, could yield the same information as these phase-3 studies and answer these research questions faster, according to Weaver. "But frankly, there are a lot of people invested in the phase-3 model," he said.

Comparative-effectiveness research

Soon, another research model may become more standard. In the American Recovery and Reinvestment Act, passed in February 2009, $1.1 billion was allocated for comparative-effectiveness research. Unlike placebo-controlled trials, comparative-effectiveness research is designed to compare the efficacy of two active therapeutic approaches, which is a far more appealing strategy to patients, according to Baker.

"In addition, the recently passed health care reform legislation established a non-profit organization called the Patient-Centered Outcomes Research Institute that will identify research priorities and conduct research that compares the clinical effectiveness of medical treatments," said Nancy Davenport-Ennis, founder and CEO of the National Patient Advocate Foundation and the Patient Advocate Foundation.

However, not all of the response to comparative-effectiveness research has been positive. Concerns exist that insurers will be able to use the results of these trials to deny patients coverage of certain treatments.

"I am concerned that the health care bill is designed to deny access to cutting-edge therapy," Weaver said. "'Comparative effectiveness,' what does that mean? Most of the stuff in this bill has to do with cost efficacy, and improving access to care, not improving clinical outcomes.

"If your goal is to improve coverage, than cost-effectiveness is important because the cheaper you can deliver therapy, the more people you can give therapy to without breaking the system. However, as a patient advocate, I am more interested in improving patient outcomes than societal cost-effectiveness," Weaver said.

Davenport-Ennis said she is also concerned about the line between cost-effectiveness and clinical effectiveness.

"Comparative-effectiveness research is a necessary step in the

nation's move to control cost and spending while assuring that what a patient is paying for is resulting in quality health care delivery, which right now does not necessarily happen," she said.

"It's a step in the right direction. As we take these steps, we all have to be committed to the greater good, to making certain that if you become ill, you will have access to the therapy that your doctor defines as the most appropriate for you, and that your access will not be limited because a comparative-effectiveness research study drew a cost line between one therapy and another, and your insurance company used that information to decide what was the best therapy for you."

"The non-profit patient community is interested to see that we look at comparative-effectiveness research as a mechanism to help a patient and doctor make a better decision about which clinical intervention would offer them the greatest hope of stopping the disease or controlling the disease," Davenport-Ennis said.

"When we look at that, we look at comparative-effectiveness research as needing to be built on the shoulders of clinical evidence."

Future directions

Reaman said in many ways, physicians have been doing comparative-effectiveness research for decades, and it is too soon to predict the overall effect of this legislation. However, addressing the lack of enrollment is crucial to the success of clinical trials, regardless of whether they are placebo-controlled research or comparative-effectiveness research.

The health care reform bill has a provision that ensures payment for routine care cost for patients enrolled in clinical trials, Davenport-Ennis said. "Right now, for many patients, their insurance will not pay for those routine costs associated with their participation in clinical trials."

This legislation is a step in the right direction, she said.

In the end, improving the clinical trials process will require a complex, multifaceted approach.

"You have to make it easier for physicians to perform trials and to want to perform trials," Weaver said. "On the other side of the equation, you have to find ways to educate patients on the appropriate role of trials in their disease management and get them to be more active in that process.

"There is obviously not a simple solution to the problem because no one has solved it yet," he said.

Source: ZERO-The Project to End Prostate Cancer

Boston University Study for Gay Male PCa Survivors

There is a quality of life, post treatment study for gay male PCa Survivors being done under the auspices of the National Cancer Institute . Treatment must have been performed at least a year ago to qualify. Recruitment will be at least through the end of December of this year and possibly through January of next. There is a modest stipend for completing the review.

Further information is available on line at http://www.gayprostatecancersurvey.com or you can call or write:

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New Targeted Therapy for Advanced Prostate, MDV3100, Safe and Effective in Early Trial

An experimental drug is showing promise for the treatment of men with an aggressive form of advanced prostate cancer. A new multicenter study has concluded that the targeted therapy MDV3100 is safe and effective for patients with castration-resistant prostate cancer (CRPC), known for its limited treatment options. The research, led by investigators at Memorial Sloan-Kettering Cancer Center, appears early online and in an upcoming edition of The Lancet.

According to the findings of the Phase 1-2 study, MDV3100 shrank patients' tumors, lowered PSA (prostate-specific antigen) and stabilized disease that had spread to soft tissues and the bone. The drug also reduced the number of circulating tumor cells in the blood.

"We were encouraged to see antitumor activity in men whose disease had spread to other parts of the body after either becoming resistant to previous hormone treatments or progressing following chemotherapy," said the study's lead author Howard Scher, MD, Chief of the Genitourinary Oncology Service at Memorial Sloan-Kettering. "These findings strengthen the drug's potential to change the outlook for a group of patients who currently have limited effective treatment options from which to choose."

According to the research, MDV3100 slows tumor growth and induces tumor cells to die in men with CRPC. Although this advanced stage of prostate cancer is defined by resistance to standard therapies used to lower or block those hormones, the cancer cells actually may still depend on male hormones to grow. MDV3100 works by blocking testosterone from binding to the androgen (male hormone) receptor, stopping the movement of the androgen receptor to the nucleus of prostate cancer cells, preventing the receptor from binding to DNA, and inducing cancer cell death, even when the expression of the androgen receptor is elevated.

"This study validates what our preclinical studies have suggested: that sustained androgen receptor signaling drives CRPC and that a substantial number of CRPC tumors that progress despite multiple hormone and chemotherapy treatments remain dependent on androgen receptor signaling for growth," said study co-author, Charles Sawyers, MD, Chair of Memorial Sloan-Kettering's Human Oncology and Pathogenesis Program and a Howard Hughes Medical Institute investigator.

The drug was co-invented by Dr. Sawyers and Michael Jung, PhD, Professor of Chemistry at the University of California, Los Angeles. Their research originally demonstrated that CRPC cells have increased expression of the androgen receptor and that elevated expression of this receptor may contribute to disease progression due to a developed resistance to hormone treatment. Their collaboration led to the discovery of a number of nonsteroidal, small molecule antiandrogen compounds, including MDV3100.

In the current study, 140 patients were treated with doses of MDV3100 ranging from 30 to 600 mg daily. PET imaging, bones scans, and blood tests were used to assess the antitumor effects of the drug, which were observed at all dosages. Investigators reported declines in PSA of at least 50 percent in more than half of the patients and tumor regressions in 22 percent of the patients. Overall, two-thirds of patients had partial remissions or stable disease in tumors that had spread to soft tissue or bone.

The findings also showed that the number of circulating tumor cells fell in 49 percent of patients, and 91 percent of patients who initiated therapy with favorable counts retained favorable counts during treatment. This is important because previous research shows that changes in circulating tumor cell counts after treatment were more predictive of survival than were changes in PSA, with favorable post-

treatment counts associated with a 21-month median survival.

The drug was generally well tolerated, with nausea, constipation, diarrhea, and anorexia being the most common mild side effects reported. The most frequently reported Grade 3 side effect at higher doses was fatigue. The researchers determined that the maximum tolerated dose for sustained treatment was 240 mg daily.

Source: psa rising

Amgen's Prolia Clears EU; U.S. Nod Expected Shortly

by Jennifer Boggs | BioWorld | 06.01.2010

The drug widely considered to be Amgen Inc.'s future growth driver won its first approval Friday, picking up a European nod in osteoporosis, even as analysts and investors await the expected FDA approval in July as well as detailed data in oncology settings slated for presentation at the upcoming American Society of Clinical Oncology meeting.

Prolia (denosumab), a RANK ligand inhibitor, was approved in all 27 European Union member states plus Norway, Iceland and Liechtenstein for use in postmenopausal women at risk of fractures and for bone loss due to hormone ablation treatment in men with prostate cancer. It will be co-marketed with London-based GlaxoSmithKline plc under the companies' 50-50 profit-sharing deal.

The label contained no surprises and was in line with the earlier positive opinion from the Committee for Medicinal Products for Human Use, said Amgen spokeswoman Kerry Beth Daly, adding that Prolia would be made available to patients in the EU "on a country by country basis."

Amgen has not yet disclosed pricing, expected to be "a key data point," likely serving as a "proxy for eventual U.S. pricing," noted analyst Christopher Raymond, of Robert W. Baird & Co., especially for the potential oncology setting, which calls for a higher and more frequent dosing regimen.

Prolia's recommended dose in osteoporosis is 60 mg via subcutaneous injection twice yearly, while the oncology setting has tested the monoclonal antibody administered at 120 mg every four weeks.

The EU approval primarily was based on data from two pivotal studies. The three-year FREEDOM (Fracture REduction Evaluation of Denosumab in Osteoporosis every six Months) study in 7,808 women with postmenopausal osteoporosis showed that those receiving Prolia experienced a 68 percent reduction in the relative risk of suffering a new vertebral fracture compared to those on placebo.

Results from the HALT (Hormone Ablation Bone Loss Trial) study in 1,468 men undergoing androgen-deprivation therapy for nonmetastatic prostate cancer demonstrated that those on Prolia had a 62 percent reduction in the risk of suffering new vertebral fractures.

In the U.S., the FDA is slated to make a decision on Prolia in PMO (postmenopausal osteoporosis) by July 25, 2010. The agency issued a complete response letter in October asking for additional trials in preventing and treating bone loss in the prostate cancer hormone therapy and breast cancer hormone therapy indications - both of which comprise relatively small markets - but required only postmarketing surveillance information in the $1 billion-plus PMO market.

But prevention of skeletal-related events (SRE) in advanced cancer represents the largest potential revenue-generator for Prolia. Standard of care in that estimated $2 billion space is Zometa (zoledronic acid) from Novartis AG, but head-to-head studies have favored Prolia.

Analysts eagerly await detailed data from a Phase III trial comparing the two drugs at the ASCO meeting in Chicago.

In addition to efficacy, observers will be looking for signs of osteonecrosis of the jaw, a side effect that turned up in earlier studies and could impact potential sales.

Thousand Oaks, Calif.-based Amgen filed a biologics license application last month for preventing SREs in cancer patients.

Source: ZERO-The Project to End Prostate Cancer

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If you need or want to help:

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